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EUROPEAN SOCIETY OF ANAESTHESIOLOGISTS ANNUAL CONGRESS ABSTRACTS

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9-12 FEBRUARY 1994

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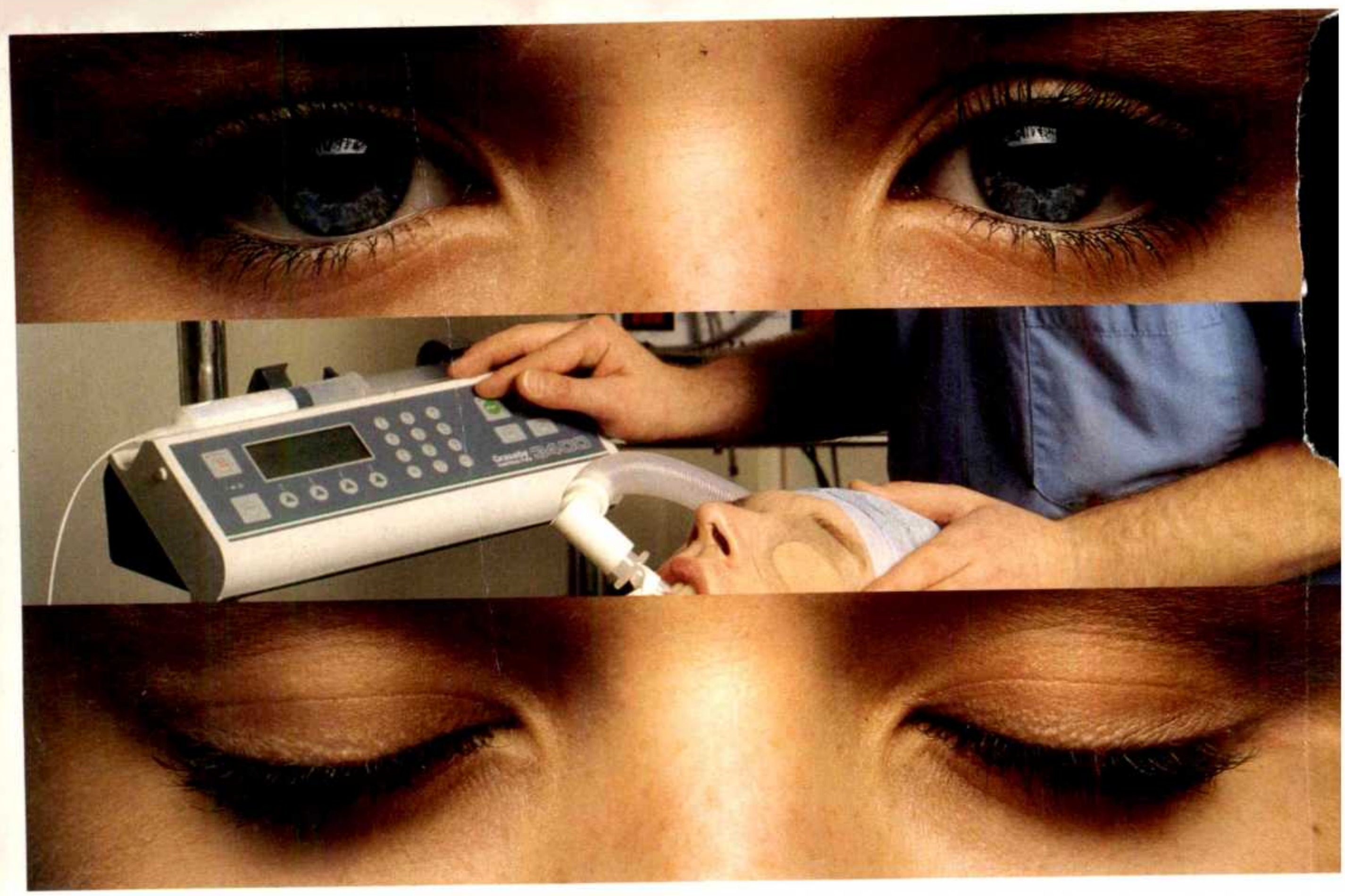
ROYAL COLLEGE OF ANAESTHETISTS



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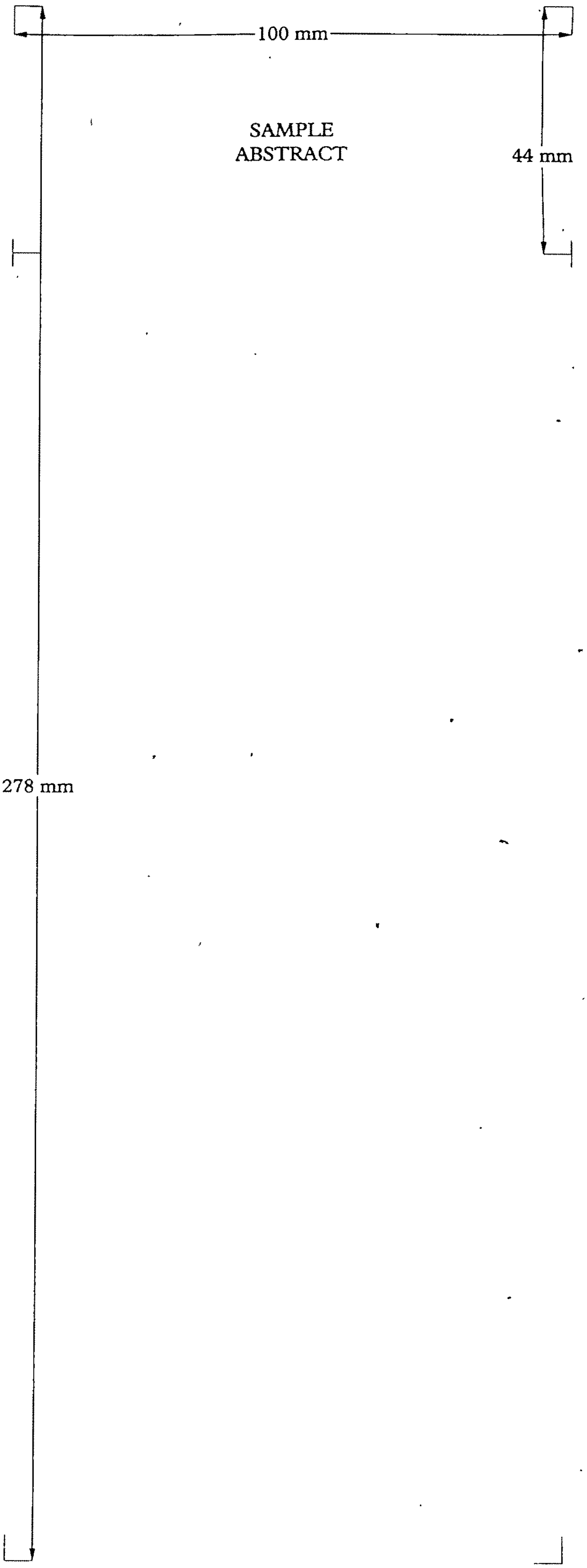

EUROPEAN SOCIETY OF ANAESTHESIOLOGISTS ANNUAL CONGRESS

9–12 February, 1994

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A.1

Influence of Aging of the Population on the Workload of an Anaesthesia Service

C.E. Klopfenstein (1), F. Herrmann (2), R. Bourdilloud (3),
A .Forster (1)
Department of Anaesthesiology (1), Institutions of Geriatrics (2), Division of Informatic (3)
University Hospital, Geneva, Switzerland

Background and goal of the study: As a result of the significant increase in life expectancy, it is assumed that anaesthetists take care more and more of elderly patients, who require, when compared with younger patients, more sophisticated anaesthetic care, in relation to the increased prevalence of age-related concomittant diseases and the decline in basic organ function in this patient population (1).
The aim of this retrospective study was to quantifiy from 1985 to 1991 the evolution of anaesthesia care of the elderly population in our institution.
Materials and methods: From the database of our institution, the following parameters of patients (>70 years) anaesthetized between 1985 and 1991 were analysed: number of patients, age, number of ASA>III, anaesthesia duration, incidence of emergency procedures, number of patients with complications during anaesthesia. The results are expressed as mean±SD and as percentage. Linear regression analysis was used to analyse the evolution of the different variables over the years.
Results : The results summarized in table 1 show a significant increase of the total number of anaesthesized patients in our institution (+ 2.26±0.59% per year), but the number of elderly increased significantly (p<0.05) more (+ 3.02 ± 0.70% per year). In the latter patient population, there is a significant increase in mean age over time, in the number of emergency patients, and in the absolute number as well in the percentage of patients > ASA III, in the duration of anaesthesia and in patients who presented a complication during anaesthesia.
Conclusions: Although our data show only a mild increase of age and of percentage of elderly patients anaesthetized between 1985 and 1991 in our institution, they clearly demonstrate that the elderly undergo proportionally longer procedures, are more often at high risk and suffer more from complications during anaesthesia than the younger population.
All these factors have thus increased quantitatively and qualitatively the workload of our institution.

References: 1. McLesky (ASA Refresher Course 1991)

Table 1

	n >70 years (% of total number of patients)	mean age (years) (±SD)	number of emergencies (% of n)	number of ASA >III (% of n)	anaesthesia duration>4h (% of n)	number of patients with complications (%of n)
1985	1965 (12 7%)	78 1 ±6 1	622 (33%)	1006 (51 2%)	516 (26%)	242 (12 3%)
1986	2180 (13 1%)	78 6 ±5 8	710 (34%)	1143 (52 5%)	613 (28%)	296 (13 6%)
1987	2357 (13 5%)	78 7 ±5 9	760 (35%)	1320 (56 0%)	756 (32%)	349 (14 8%)
1988	2263 (12 5%)	78 8 ±6 1	692 (31%)	1326 (58 6%)	799 (35%)	321 (14 2%)
1989	2328 (13 0%)	78 8 ±6 3	731 (32%)	1398 (59 8%)	894 (38%)	340 (14 6%)
1990	2420 (13 0%)	79 1 ±6 4	883 (38%)	1370 (56 6%)	950 (39%)	368 (15 2%)
1991	2458 (13 7%)	78 8 ±6 4	902 (38%)	1413 (57 5%)	850 (35%)	379 (15 4%)
r^2 | |	0 79**	0 68*	0 77**	0 80**	0 81**	0 80**
r^2 %	0 34	-	0 19	0 58*	0 75*	0 79**

n = number of patients > 70 years old
r^2 | | = linear regression coefficient of absolute data over time period
r^2 % = linear regression coefficient of percentage data over time period
* $P < 0.05$; ** $P < 0.01$

A.2

ROUTINE PREOPERATIVE SCREENING TESTS FOR INFECTIOUS DISEASES IN VASCULAR PATIENTS

M.Bertrand, L.N'Guyen[1], M.Gosgnach, JP.Cornet, S.Benkhalifa ,A.Zubicki,G.Godet,S.Mouren , P. Viars
Department of Anesthesiology,[1]Blood center ,Hopital Pitié-Salpétrière , Paris ,France

Introduction: The homologous transfusion is a life-saving procedure but is also associated with a variety of unwanted effects such as the transmission of infectious agents of which the hepatitis viruses are the most common and the HIV virus the most scaring. Since the transfusion is not the only way to contact these diseases we routinely detected them before operation ,both to inform the patients and avoid any postoperative complain for blood transmitted diseases and to permit an effective protection of the medical and paramedical staff .The aim of our study was to determine in vascular patients the percentage of those already infected.
Material and methods: We prospectively included in this study all the patients admitted in our institution for any kind of vascular procedures during a 1 year period. Before the operation these patients underwent a set of screening tests (ELISA) to detect the presence of the following agents :

- * Hepatitis B virus: HBs antigen , HBc antibody
- * Hepatitis C virus : HCV antibody
- * HIV virus : HIV I/II antibodies
- * HTLV virus ; HTLV I/II antibodies

The positive tests were controlled by a Western blot
Results: 721 consecutive patients were studied .The number of positive tests is shown in the table.

	positive tests (n)	positive tests (%)
HBs Ag	7	1%
HBc Ac	126	17.5%
HCV Ac	25	3.5%
HTLV Ac	2	0.3%
HIV Ac	0	0

Conclusion: These results confirm the low incidence of HIV and HTLV virus in a non selected population. On the other hand , we found a non negligible rate of preoperative HBc Ac in these patients but the consequences of this positive test are not totally elucidated.These results impose precautions for all medical staff. These preoperative tests allowed us to inform patients and to send them for specialized consultations.They also constitute baseline measurements of their immunologic status which are required for further determination of post transfusionnal serologic conversion.

References: Dodd ;NEJM 1992;327:419-421
Donahue & al ; NEJM 1992;327:369-373

A.3

ECHOCARDIOGRAPHIC PREDICTION OF CARDIAC COMPLICATIONS TO VASCULAR SURGERY.

P Hohner, C Backman, K Karp, S Reiz

From the Departments of Cardiothoracic Anaesthesia and Surgery and Clinical Physiology, University of Umeå, Sweden.

Background & goal of study: Cardiac ischemic complications constitute a major part of morbidity after vascular surgery (1). Preoperative indentification of patients at risk by various physiological tests has been shown difficult or unreliable (2). This study documents the ability of preoperative transthoracic echocardiography (TTE) to identify patients with perioperative cardiac events and one-year cardiac morbidity/mortality.

***Patients & methods*:** 115 consecutive abdominal vascular surgical patients with coronary artery disease were studied perioperatively and followed during the first postoperative year. A clinical history, a 12-lead ECG and a TTE were obtained preoperatively. Intraoperative cardiac events were defined as (a) ischaemia by 12-lead ECG, and/or (b) LV failure (by PCWP above 18 mm Hg, or increasing by over 30% if higher at control, and requiring iv nitroglycerine). Immediate (72h) postoperative events were defined as myocardial infarction (MI) (by ECG and enzymes), LV failure requiring inotropic or vasodilator therapy, or ischaemia (by angina or ECG). One-year cardiac morbidity included patients with postoperative cardiac events (MI, LV failure and unstable angina) and those who later suffered cardiac death, MI or worsened cardiac symptoms.

***Results*:** Preoperative TTE demonstrated LV hypokinesia and akinesia (SWMA) in 54% and 12% respectively, LV fractional shortening (FS) below 0.35 in 41%, and LV end-diastolic diameter (LVØ)≥55 mm in 32%. Intraoperatively, ischaemia was observed in 17.4% and LV failure in 50%. Postoperatively (72h), 7.8% had MI, 6.1% LV failure, 8.7% unstable angina and 30% ECG ischaemia. One-year cardiac morbidity was 31/115 (26.9%), including 4 cardiac deaths. LVØ≥55 mm predicted intraoperative LV failure ($p=0.013$, positive predictive value (ppv) 65.7%, negative predictive value (npv) 57.3%) and postoperative ischaemia ($p=0.003$, ppv 48.6%, npv 78.7%). SWMA predicted postoperative LV failure ($p=0.050$, ppv 9.2%, npv 100%) and one-year cardiac morbidity ($p=0.024$, ppv 32.9%, npv 84.6%). [SWMA + LVØ≥55 mm] predicted intraoperative LV failure ($p=0.006$, ppv 70.0%, npv 57.5%) and postoperative ischaemia ($p=0.004$ ppv 50.0%, npv 77.5%). FS below 0.35 did not predict cardiac events.

Discussion & conclusions: Our results document that absence of SWMA-s by preoperative TTE identifies a vascular surgical population at low risk for postoperative LV failure, and ischaemia, and one-year cardiac events. An increased LV diameter alone or in combination with SWMA-s is an acceptable predictor of patients at risk for intraoperative LV failure. The TTE could thus be used to identify patients who might benefit from invasive haemodynamic and/or transoesophageal echocardiographic monitoring.

***References*:** (1) Mangano DT, et al: Anesthesiology 1990; 72:153-184. (2) Bertrand et al, Anesthesiology 1990; 73:A85.

A.4

A SURVEY OF 730 000 SPINAL ANESTHESIA.

Y. Auroy, B Rouvier, K Samii*.

*Département d'Anesthésie - Réanimation, Hôpital de Bicêtre, Université Paris-Sud, 94275 - Kremlin Bicêtre, FRANCE.
Département d'Anesthésie - Réanimation, HIA Bégin, 69 Av de Paris, 94160 Saint Mandé. FRANCE.

Background and goal of study: Spinal anesthesia (SA) is considered as a simple and safe procedure of regional anesthesia. Recent informations on severe cardiovascular accidents during SA (1) have not been followed by a survey in order to estimate the safety of this procedure. The aim of this survey was to register the major accidents of SA.

Material and methods : This survey was performed through 2 steps: 1) First step: A questionnaire, previously tested by six experts and in our departement, was sent to 6000 french anesthetists; confidentiality was ensured. The 20 questions of this first questionnaire could be divided in two separate topics: a) Personal characteristics of the anesthetists, duration of their experience in SA and their estimated number of SA during the last five years. b) Number of major complications observed during the 5 last years of their experience: - Cardiac arrest that required either an ECM or epinephrine - Respiratory arrest that required either an assistance or an intubation - Cranial nerve damage (diplopy, acoustic or visual defects) - Neurologic complications such as radicular or cauda equina syndrom, meningitis, intracranial or perimedular hematoma - Death due to SA observed in the 5 past years. 2) Second step: A second detailed questionnaire, specific to each type of accident was sent to every anesthetist that reported at least one major accident in the first questionnaire. Statistical analysis included Student t test and chi 2 test as appropriate.

Results and discussion: 1100 anesthetists who had performed 730 000 SA in the last 5 years answered to our first questionnaire. 410 of them experimented at least one major accident and received the second questionnaire. A 40% response rate was obtained for the second part of the study. The complications are summarized in the table:

Complications reported for 5 years	Number
Radicular/cauda equina syndrom	160 / 42
Perimedular hematoma	14
Cranial nerve damage	232
Meningitis	22
Intracranial hematoma	8
Cardiac arrest	86
Respiratory arrest	216
Death	30

The detailed informations contained in the second questionnaire brought precise informations on the mechanism of these accidents.

Conclusion : This survey of 730 000 SA shows that the common impression of the safety of SA needs to be reevalued.

Reference : 1) Caplan et al. Anesthesiology 1988; 68: 5-11.

A.5

A COMPARISON OF APACHE-III AND APACHE-II IN ICU-PATIENTS

Th. Bein, D. Fröhlich, A. Frey, Ch. Metz, K. Taeger
Clinic of Anesthesia, University of Regensburg, 93042 Regensburg, Germany

INTRODUCTION: Scoring systems, like Acute Physiology And Chronic Health Evaluation (APACHE-II, APACHE-III) are used in intensive care medicine to classify the severity of illness and to predict the outcome. The prognostic value of these scores has been demonstrated on large data bases (1,2). APACHE-III, introduced in 1991, has not been validated in Europe until today. We calculated APACHE-II and APACHE-III in a general intensive care unit (ICU) and evaluated the capacity of the prognosis of hospital outcome.

METHODS: Between July 1992 and June 1993, 290 patients were treated in the ICU. For enrollment into the study, the time span of treatment had to exceed 24 h (= 150 patients). We calculated APACHE-II and APACHE-III as described by the authors and compared the mean and median values of the survivors with the nonsurviving group (Mann-Whitney-U-test). Receiver-operating characteristics (true positive rate versus false positive rate: "ROC-analysis") were plotted for both scores and the areas under the ROC-curves were calculated.

RESULTS: 34/150 patients (= 22,5 %) died during hospital stay. The mean time of treatment was 9.9 ± 12.5 days. The mean and median values of the scores were significantly higher (p<0.001) in the nonsurviving group (table 1).

	survivors	nonsurv.	
APACHE-II:			
mean	16.4±5.8	24.5±5.6	
median	17	24	***
APACHE-III:			
mean	41.9±20.3	76.6±21.1	
median	40	74.5	***

table 1: *** = p< 0.001

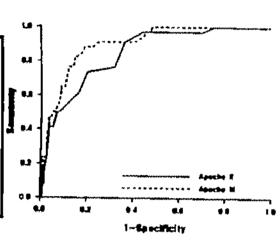


figure 1

The area under the ROC-curve (fig. 1) was 0.899 (APACHE-III) in comparison to 0.847 (APACHE-II).

DISCUSSION: APACHE-II and APACHE-III were found to have a good prognostic value in general ICU-patients. Our results suggest that the new APACHE-III-version includes a more accurate disease classification and a more precise prediction of hospital mortality than APACHE-II. It is to investigate if new scoring systems will do the job of risk stratifying in critically ill patients in Europe.

REFERENCES: 1. Knaus WA, Draper EA, Zimmerman JE et al.: Crit Care Med (1985) 13:818. 2. Knaus WA, Draper EA, Zimmerman JE et al.: Chest (1991) 100:1619

A.6

CLINICAL PREDICTORS OF THE NEED FOR A PREOPERATIVE MYOCARDIAL REVASCULARISATION IN PATIENTS UNDERGOING AORTIC SURGERY

**Coriat P, Bertrand M, Gosgnach ML, Buy E,
Zubicki A, Viars P**

**Department of Anaesthesia, Pitié-Salpêtrière Hospital
75013 Paris, France**

Myocardial revascularisation (MR) (Coronary artery bypass grafting or angioplasty) has assumed an increasing role in the preoperative preparation of patients undergoing aortic surgery. The aim of this study was to determine the clinical predictors of the need for preoperative M.R. in this population.

Methods : During a three year period 1991-1993, patients aged between 55-71 years admitted to our institution for abdominal aortic surgery were studied. Coronary angiography was performed in these consecutive patients as part of their preoperative assessment. In patients studied during 1991-1992 we used a backward forward stepwise logistic regression model to determine which preoperative findings were independently and significantly related to the need for MR. The predictive values determined using this logistic model were compared with the data observed in the 1993 population.

Results : Prevalence of CAD in the two populations :

	1991-1992	**1993**
n	202	55
age (year)	59	61
Coronary stenosis > 50 %	55 %	49 %
PTCA & CABG	15 %	18 %

Variable associated with MR among patients studied during 1991-1992 :

	Odds Ratio	**p value**
age > 59 years	3,3	p < 0,004
Clinical CAD (1)	2,3	p < 0,02
AAA (2)	2,0	p = 0,05

(1) Angina or previous MI.; (2) aneurysm vs occlusive aortic disease

Comparison of predicted positive value (1991-1992) and observed responses in 1993

AAA	> 59 y	CAD	Predicted 1991-1992	Observed 1993
yes	yes	yes	68 %	66 %
yes	yes	no	29 %	20 %
no	yes	no	14 %	12 %
no	no	no	4%	6 %

Conclusion : Our data allow to establish a simple, rational algorithm to appropriately select patients in whom a coronary angiography should be ordered before AA surgery.

A.7

MYOCARDIAL REVASCULARISATION BEFORE CAROTID SURGERY

J. Maintenant, M.H. Fléron, E. Buy, A. Zubicki,
P. Coriat, P. Viars
Département d'Anesthésie-Réanimation, G.H. Pitié-Salpêtrière, 75013 Paris, France

Coronary artery disease (CAD) is responsible for over 50 % of immediate, medium and long term mortality following carotid surgery. This implies that identification of significant CAD is important in this population despite the low immediate post operative cardiac morbidity. With development of coronary angioplasty, there has been an increased interest in identifying vascular patients who might benefit form myocardial revascularisation (MR) prior to surgery.

The aim of this study is to determine the clinical parameters associated with an indication for preoperative MR in patients scheduled for carotid endarterectomy.

Methods : All patients (n = 104) aged between (50-71 y) (mean age 62 y) admitted to our institution for carotid endarterectomy during 1992-1993 were prospectively studied. Besides the standard preoperative evaluation they all underwent a coronary angiography before carotid surgery. The indication for a MR was determined by an in dependent cardiologist.

We used a backward forward stepwise logistic regression model to determine which clinical parameters were independently and significantly related to 1) the presence of a coronary artery stenosis, 2) an indication for a preoperative MR

Results : 30/104 pts had a clinical CAD (angina or previous MI), at least one coronary artery stenosis > 50 % was found in 65 pts, a MR was indicated in 13 (CABG n=8, angioplasty n=5) Clinical parameters associated with the presence of at least one coronary artery stenosis > 50 % are :

	Odds Ratio	**p value**
age > 65 years	3,0	0,01
Clinical CAD	4,7	0,005
Diabetes + insulin	5,7	0,113

Only one clinical preoperative parameter was associated with the need for MR :

	Odds Ratio	**p value**
Clinical CAD	8,9	p < 0,003

Conclusion : Preoperative clinical predictors of the presence of CAD and those associated with an indication for MR must the taken into account to select among patients scheduled for coronary angiography those in whom a MR is indicated. This may avoid the prescription of an excessive number of unnecessary coronary angiography.

A.8

IATROGENIC NON SURGICAL BLOOD LOSSES IN ADULT CARDIAC SURGICAL PATIENTS

Patricia Lavand'homme, Agnès Masson, Philippe Baele

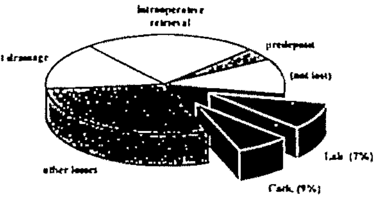
Department of Anaesthesiology, UCL Medical School, St Luc Hospital, 1200 Brussels, Belgium.

Background and goal of study : Efforts towards blood conservation should tend to decrease blood losses, optimize the use of allogeneic (allo) resources and promote autologous (auto) transfusions. Non surgical medical interventions constitute a source of blood losses which has received little attention in patients undergoing surgery. This study focuses on losses linked to cardiac catheterisation (cath) and laboratory (lab) sampling.

Materials and methods : In 142 consecutive patients, besides anthropometric and evolution data, the following variables were collected retrospectively from computerized lab and blood bank files, and from medical records : volumes lost to lab sampling, volumes of chest drainage, haematocrit (Hct) before and after cath, Hct on admission to and discharge from the surgical unit, volumes of transfused auto and allo blood. Volumes of blood lost during cath and uncompensated losses endured during surgery were computed from relevant changes in Hct, according to standard formulas⁽¹⁾.

Results : On the average cardiac surgical patients lost 89 % of their initial red cell mass (iRCM), i.e. 1674 ml (range 200 to 4416 ml). The figure shows the various blood losses expressed in % of the initial red cell volume of the patient. (Quantities are expressed as mls of 100 % Hct erythrocytes). Losses linked to predeposit were 76 ml (4 % of iRCM); cath 137 ml (7 %; range 3 to 29 %); lab 173 ml (9 %; range 4 to 21 %); chest drainage 289 ml (15 %); intraoperative blood retrieval 445 ml (24 %) and non documented blood losses (e.g. sponges, residual oxygenator blood, hemothoraces ...) 554 ml (30 %).

% of Initial Red Cell Mass



On the average 761 ml allo blood were transfused (43 % iRCM). The following variables increased (Multiple regression analysis) lab losses : hospital stay (p < 0,0001), ICU stay (p < 0,0001), bypass time (p = 0,0002), preexisting renal failure (p = 0,0006), reopening for ischemia (p < 0,002), aprotinine use (p < 0,02), diabetes mellitus (p < 0,05).

Conclusion : Medical non surgical interventions, such as cardiac cath and lab sampling, provoke substantial blood losses in surgical patients. Comprehensive strategies should be developed to address this question in order to minimize unnecessary transfusions.

Reference : ⁽¹⁾ Toy and al. Transfusion 1992; 32 : 63-67

A.9

HOMOLOGOUS BLOOD TRANSFUSION AS A RISK FACTOR FOR POSTOPERATIVE INFECTION AFTER ABDOMINAL AORTIC SURGERY

M Bertrand, JF Baron, M Gosgnach, MH Fléron, G Godet,
S Mouren, M Ismail, E Kieffer, P Viars

Departments of Anaesthesiology - Hôpital Pitié-Salpêtrière
and Hôpital Broussais - Paris France

Extensive data suggest that homologous blood transfusions have immunosuppressive effects on recipient including increased risk of postoperative bacterial infections (1). Few clinical studies have been designed specifically to examine the relationship between homologous transfusion and infection rate. We also examine the relationship with cardiac and respiratory complications.

Methods : During a 5 years period, we reviewed the medical records of 872 consecutive patients who underwent abdominal aortic surgery. These files initially stored to study predictors of cardiac complications also included infection and transfusion data. All variables have been defined prospectively. Preoperative evaluation included usual clinical variables. Inclusion in a predonation program (n = 496) was performed with usual contraindications and limitations. A cell-saver was selectively used intraoperatively when blood loss in a sterile reservoir were greater than 1500 ml. Postoperative myocardial infarction, and congestive heart failure were defined using standard criteria. Pneumonia was defined as the new appearance of an infiltrate on chest x-rays associated with a temperature >38.5 °C and elevated WBC count. Acute respiratory failure was defined as need for mechanical ventilation for more than 24 h. General sepsis was defined by the presence of a localized infection with clinical evidence of bacteremia and at least one positive blood culture. Infection could be minor (local) or major (sepsis or pneumonia).

Using appropriate parametric or non parametric tests, we compared patients who received homologous blood products with those who did not.

Results : Preoperative cardiac disease were more frequent in patients transfused with homologous blood. The rate of cardiac, respiratory complications and infections was significantly higher in patients who received homologous blood

	Homologous - n = 417	Homologous + n = 455
Preoperative Evaluation		
Myocardial Infarction	55 (13 %)	81 (18 %)
Angina	57 (14 %)	91 (20 %) *
Left Ventricle Insuffisency	8 (2 %)	25 (5 %) **
COPD	170 (42 %)	193 (45 %)
Creatinine > 150 µmol/l	45 (11 %)	108 (23 %) ***
Diabetes Melitus	33 (9 %)	45 (11 %)
Postoperative Complications		
Myocardial Infarction	4 (1 %)	21 (5 %) **
Left Ventricle Failure	7 (2 %)	36 (8 %) ***
Pneumonia	35 (8 %)	85 (19 %) ***
Respiratory Failure	6 (1 %)	56 (12 %) **
Renal Failure	11 (3 %)	50 (11 %) ***
General Sepsis	8 (2 %)	37 (8 %) ***
Infection (minor or major)	105 (25 %)	173 (38 %) ***
Postoperative Death	3 (1 %)	40 (9 %) ***

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ between groups.

Conclusions : Homologous transfusion is an important risk marker for postoperative bacterial infections and other complications, but causality is more difficult to establish.

Reference : (1) Murphy PJ, J Thorac Cardiovasc Surg, 1992, 104 : 1092-1099

A.10

POST CARDIAC SURGERY INFECTION RATE AFTER AUTOLOGOUS OR HOMOLOGOUS TRANSFUSION

F. BERGAOUI*, L. PIPIEN*, J.-N. FABIANI**,
S. MASSONNET-CASTEL***, M.-Th. COUSIN*

Service d'Anesthésie*, Chirurgie Cardiaque**
et de Transfusion***,
Hôpital Broussais, 96, rue Didot, 75014 PARIS, FRANCE.

Numerous infection factors are involved during cardiac surgery. Homologous transfusions have been said to increase post operative infection rates (1). However, the role of blood transfusions have not yet been fully elucidated. The aim of this study was to assess homologous influence on postoperative infection rates as compared to autologous transfusion.

METHOD

In 1992, 135 patients (pts) underwent coronary artery bypass grafting (CABG) by the same surgeon. Two groups (gr) were retrospectively formed : gr A, with 2 to 3 units of pre-operative autologous blood predonations and gr H, who received homologous blood products. Emergencies, pts with recent myocardial infarction, and pts with renal and respiratory diseases were excluded. All pts received preventive antibiotics (Cefazolin). Bacterial infection was assessed by an independant comittee. The criteria for infection was set at two consecutive days of fever associated with positive cultures during the following 10 post operative days.

RESULTS

Gr A (n = 36) and gr H (n = 26) did not differ in age, functional class, graft number, CPB duration, number of packed RBC's transfused and postoperative hemodilution. Although not significant, lower infections rates were observed in gr A compared to gr H (Table I).

DISCUSSION

No serious infections (mediastinitis and septicemia) were observed. Infections were essentially superficial wound infections and minor lung infections. In gr H, pts were carefully selected to match with gr A pts. To reach a significant statistical difference , a larger number of patients, more than could be operated in one year by one attending surgeon, would be necessary. Numerous factors such as duration of the study, multiple surgeons, environnemental microbial infection rate, etc. would then obscure the protocol.

However, the above favorable preliminary results lead us to encourage and to enlarge the number of patients enroled in our autologous transfusion programm.

Table

	Gr A	Gr H	Total
n	36	26	62
No infection	33 (92 %)	22 (85 %)	55 (89 %)
Infection	3 (8 %)	4 (15 %)	7 (11 %)

REFERENCE

Transfusion, 1991, 31, 212-217.

A.11

A COMPARISON BETWEEN KETORALAC OR DICLOFENAC AS AN ADJUNCT TO ANAESTHESIA FOR SHORT OUT-PATIENT PROCEDURES

Jan Jakobsson, Kerstin Rane.
Department of Anaesthesia,
the Karolinska Institute at Danderyd´s Hospital,
18288 Danderyd, Sweden.

Nonsteroidal antiinflammatory drugs (NSAIDs) are effective analgetics that are devoid of opioid-related side effects and may prove useful for short outpatient procedures.

Aim of the study

This randomized, double-blind study was designed to compare the perioperative analgesic efficacy, recovery times, and postoperative side effects when ketoralac or diclofenac were administered to out-patients undergoing minor gynecologic procedures.

Methods

Two hundred ASA class I patients sceduled for termination of pregnancy in general anaesthesia were randomly divided into four groups receiving; 30 mg ketoralac im, 75 mg diclofenac im, 50 mg diclofenac orally or 2 ml NaCl im short before induction of anaesthesia. All patients were anaesthetized with 0.5 mg alfentanil, thiopentone and breathed oxygen in nitrous oxide 1:2 during the procedure. Amount of induction agent, need for postoperative analgetics and time to discharge were registered. At discharge all patients were asked to answer a questionnaire concerning quality of anaesthesia.

Results

All patients had an uncomplicated course. No case of recall of intraoperative events was noticed. The results are presented in the table.

	thiopentone + alfentanil 0.5 mg			
	diclo.po (n=50)	diclo. im (n=50)	ketor. im (n=50)	NaCl im (n=50)
amount of induction agent (mg/kg)	8.1±1.6	7.8±1.8	7.7±1.7	7.8±1.5
pain / no pain	16 / 34	7 /43	6 / 44	16 / 34
nausea/vomiting	4 / 4	0 / 3	2 / 1	4 / 2
analgetic requirement (No pat)	23	13	12	23
time to discharge (min.)	109±29	109±24	107±27	123±40

Conclusion

- the addition of ketoralac 30 mg or diclofenac 75 mg im improved the postoperative paincourse in the same fashion, and more than oral diclofenac or placebo

- the addition of NSAIDs did not shorten time to discharge nor did it make any difference to the amount of induction agent needed

A.12

PREMEDICATION, A COMPARISON BETWEEN TEMAZEPAM, KETOBEMIDONE, PROPRANOLOL AND PLACEBO.

Jan Jakobsson, Kerstin Rane, Gudrun Ryberg
Department of Anaesthesia,
the Karolinska Institute at Danderyd´s Hospital,
18288 Danderyd, Sweden.

Background

There is no "gold standard" for premedication, and the routines and drugs given varies considerably between different hospitals.

Aim of the study

To compare three different drugs with anxiolytic and sedative properties given orally in a dubble-blind randomized fashion to placebo.

Methods

One hundred and twenty patients in four groups were randomly assigned to receive temazepam 1 mg, ketobemidone 5 mg, propranolol 40 mg or placebo orally 30 - 90 minutes prior to anaesthesia. Patients self assessment of the effects of premedication, observers evaluation, amount of and complications during induction and the postoperative course have been studied.

Results

The groups were comparable in terms of patients characteristics, duration of surgery and anaesthesia.The results are presented in the table.

drug	placebo (n=30)	propran. (n=30)	temazep. (n=30)	ketobemid. (n=30)
Patients evaluation of anxiety more/unchanged/less	5 / 15 / 10	8 / 17 / 5	7 / 14 / 9	7 / 12 / 11
Observers evaluation adequate / inadequate	22 / 8	19 / 11	20 / 10	26 / 4
Induction;				
pulse	76±7	71±9	77±2	75±9
blood pressure (mmHg)	125±15	117±14	120±113	123±15
induction agent (mg/kg)	5.6±1.1	5.4±0.8	5.4±1.0	5.8±1.2
Postoperative;				
analgesic requirement	21	17	17	19
nausea/vomiting	11/0	11/7	6/5	7/3

Conclusion

We found no major differences between the three active drugs tested or placebo,
- in regard to patients or nurses evaluation
- in regard to pulse and blood pressure at induction or the amount of induction agent needed
- in regard to the postoperative-course

A.13

Anaesthetic Preoperative Assessment in Out Patient Clinic

A Survey of the Opinion of Anaesthetists, Surgeons and Hospital Directors in Switzerland

C.E. Klopfenstein, I. Schwieger, D.R. Morel, A. Forster
Department of Anaesthesiology,
University Hospital, Geneva, Switzerland

Background and goals of the study: In Switzerland, anaesthetists have no opportunity to consult their patients before hospital admission, resulting in longer preoperative hospitalisation and last minute cancellation of the operation because futher investigation is required.Preoperative Assessment in Out Patient Clinic (*APAO*) is an early preoperative consultation in ambulatory facilities. The aims of the *APAO* are to improve anaesthetic care by allowing a better preoperative assessment and to lower the health costs by reducing duration of the period between hospital admission and surgery, and decreasing last minute cancellation of elective surgery.

The goals of the study were to determine the opinion of anaesthetists, surgeons and hospital directors on the *APAO* and to evaluate the needs and the problems related to *APAO*

Materials and Methods: A questionnaire was sent to 100 anaesthetists, 100 surgeons and 74 hospital directors working in the French part of Switzerland. The collection of the data was anonymous

Results and discussion: Surprisingly significantly less anaesthetists than hospital directors and surgeons (64% vs 75% and 72%) responded to the survey; however significantly more anaesthetists and surgeons than hospital directors were interested in the *APAO* (96% and 92% vs 79%). As summarized in table 1, significantly more anaesthetists than surgeons think that *APAO* can improve hospital management and OR performance. The administrative and financial difficulties are more often stated by anaesthetists as the limitating factor of *APAO*-activity.

Table 1 Benefits and Problems related to APAO

	reduced hosp-stay	*increased OR performance*	*administr problem*	*financial problem*
director (n 55)	43,5%	60,4%	28,9%	39,5%
surgeon (n 72)	39,4%	40,0%	53,0%	24,2%
anaesth (n 64)	62,9%	77,4%	60,0%	55,0%

* $p < 0,05$ ** $p<0.01$

Conclusion: The high percentage of answers demontrates the interest in *APAO*, of the participiants. The interested anaesthetists are more aware than the others that *APAO* can partly solve hospital management difficulties and lower hospitalisation costs. *APAO* performed by anaesthesists should thus be recognised by hospital managers and insurances, as for out patient activity performed by other medical specialities. In addition, training in anaesthesiology should include *APAO* to sensitize anaesthetists to this approach

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Guilmet C. *Agressologie*, 1976, 17: 125-134
Janesko M et al *Der Anaesthesist*: 1983, 32: 174-176
Conway J.B. et al. *Can J Anaesth*: 1992, 39:10,1051-7

A.14

RECOVERY FROM SEVOFLURANE AND ISOFLURANE AFTER OUTPATIENT GYNAECOLOGICAL LAPAROSCOPY

H. Kallela, M.D., J. Haasio, M.D., K. Korttila, M.D.

Women's Hospital, Dept. of Anaesthesia,
University of Helsinki, Finland

Introduction: We compared recovery after sevoflurane and isoflurane in patients undergoing outpatient gynaecologic laparoscopy.

Methods: After approval of the Ethical Committee of the Hospital 50 consenting ASA I-II women were included in the study. The patients were randomised to receive either sevoflurane or isoflurane. Premedication was 5 mg of diazepam p.o. Prior to induction with propofol (2 mg/kg + 0.5 mg/kg PRN) the patients received 0.2 mg of glycopyrrolate, 0.1 mg of fentanyl and 0.6-0.8 mg of vecuronium i.v. Intubation was facilitated with 1.5 mg/kg of suxamethonium i.v. and vecuronium used thereafter. Maintenance of anaesthesia was started with 0.5 MAC of the study drug (EtSevof 0.6% and EtIsof 0.5%) in 67% nitrous oxide in oxygen. The end-tidal concentration of the study drug was kept in 0.5 MAC, but adjusted in 0.5 MAC steps in a standardised fashion, if needed. $EtCO_2$ was maintained between 5.0-5.5%. 5-10 min before the estimated end of the anaesthesia, the end-tidal concentration of the volatile agent was reduced to 0.25 MAC. By the time of the last skin suture 2.0 mg of neostigmine and 0.4 mg of glycopyrrolate were given i.v. and the study drug and nitrous oxide were turned off. Side effects, recovery, and achievement of home readiness were assessed. Chi-Squared and Mann Whitney U tests were used for statistical analysis.

Results: Main preliminary results [median (range)]

Parameter	Sevoflurane	Isoflurane
Age (yrs)	30 (23-39)	31 (22-39)
Weight (kg)	58 (49-78)	60 (45-71)
Durat. of anaesth. (min)	39 (16-97)	30 (18-122)
End-tidal conc. adjusted	29%	12%
Opens eyes (min §)	2.3 (0.8-7.0)***	4.1 (2.0-6.8)
Orientated (min §)	2.8 (1.0-6.8)**	4.7 (2.2-8.4)
Sitting (min §)	33 (15-88)	34 (17-93)
Oral fluids (min §)	37 (15-88)	35 (19-161)
Walking (min §)	72 (24-464)	66 (35-134)
Able to void (min §)	281 (96-708)	217 (52-591)
Home ready (min §)	281 (96-708)	242 (96-591)
Emesis (PONV) in hospital	75%	60%
Antiemetic given	46%	28%
No PONV during 24 hrs	17%	36%
Unanticipated admission to hospital	13%	16%

** = $p < 0.01$, *** = $p < 0.001$ vs isoflurane
§ = after discontinuation of the volatile agent and N_2O

Discussion: Although immediate recovery was faster after sevoflurane, home readiness was achieved as fast as after isoflurane. PONV contributed in both groups to some patients being admitted to hospital overnight.

A.15

EMERGENCE CHARACTERISTICS AFTER SEVOFLURANE VERSUS PROPOFOL ANAESTHESIA IN ADULT OUTPATIENTS

Ch. Wandel, S. Neff, H. Böhrer, J. Motsch,
A. Bach, E. Martin

Department of Anaesthesia, University of Heidelberg,
D-69120 Heidelberg, Germany

Introduction: The new inhalational anaesthetic sevoflurane is characterized in comparison to the current anaesthetics by its low blood-gas partition coefficient of about 0.69 (1). Therefore sevoflurane would seem suitable for day-case surgery. The aim of this study was to compare the emergence of ASA I and II day-case patients after sevoflurane or propofol anaesthesia.

Patients and Methods: After institutional approval and informed consent 50 patients were included in this prospective, randomized study. The investigated parameters were defined as: Period of time between the end of anaesthesia and extubation, ability of the patient to open his eyes, to squeeze hands and to say his date of birth on demand. Before and at quarter-hourly intervals over two hours after anaesthesia the patient was asked to fill in the Visual Analogue Scale (VAS) concerning awareness, energy, confusion, coordination, nausea and pain. The Digit Symbol Substitution Test (DSST) was performed at the same time. In addition, the modified Aldrete score was done every ten minutes during the first postoperative hour. For statitistical analysis, the Student's t test was used.

After induction of anaesthesia with propofol, group I (n=25) received sevoflurane for maintenance of anaesthesia in inspiratory concentrations of up to 3 vol%, group II (n=25) was given 0.1-0.2 mg/kg/min propofol. The dose was aimed to keep the blood pressure within a range of 20 % of the value, which was measured immediately before surgical incision. In each patient, the administration of the anaesthetics sevoflurane or propofol was stopped at the same time of the last skin suture.

Results: The demographic data were simillar in both groups. The periods of time between end of anaesthesia and the described events are summarized in the table (*p<0,01):

Time Interval (min±SD)	Extub.	Eye opening	Squeezing hands	Telling the date of birth
Sevofl.	6 6 ± 1.8*	7 2 ± 2.1*	8.2 ± 2.7*	8.6 ± 2.5*
Propofol	9.8 ± 6.4*	12.6 ± 8.8*	13.8 ± 10.7*	14.6 ± 10.5*

No significant difference was seen in VAS concerning awareness, confusion and coordination. The patients in the sevoflurane group felt fitter and more energetic (p<0.05), were calmer but suffered more sickness (p<0.05). In the DSST, there was a statistical signifance of p<0.01 in favour for the propofol group. The modified Aldrete score showed significantly more favourable results in group I, with p<0.01 at 10 min after the operation and with p<0.05 later on.

Conclusions: Our study confirmed the rapid emergence of patients after sevoflurane anaesthesia (2). Sevoflurane may thus prove to be a useful anaesthetic agent for day-case surgery.

References:

1. Strum DP, et al.; Anesth Analg 1987; 66:654-656.
2. Fnnk EJ, et al.; Anesth Analg 1992; 74: 241-245.

A.16

INTRAOCULAR PRESSURE AND GYNECOLOGICAL LAPAROSCOPY

J. Claude Ducloy, A. Sophie Ducloy, Eric Buy, Gilles Theeten,
B Delepine, D Vinatier, Renée Krivosic-Horber

Department of Anesthesiology, Hôpital B, CHRU,
59037 Lille cedex, FRANCE

Background and goal of study : Laparoscopy has been contra-indicated in glaucoma. Intraocular pressure (IOP) has been mesured 14 times during laparoscopy and parameters influencing IOP have been determined.

Materials and methods : the prospective study included 40 patients, who underwent gynecological laparoscopy. IOP was measured by mean of Perkin's aplanation tonometer 14 times : **1:** before induction of general anaesthesia, **2:** 5 minutes after induction, **3,4 and 5:** 5,10,15 degrees of trendelenburg position, without gynecological position, **6,7,8 and 9:** 0,6,10,12mmHg of intraabdominal pressure by CO2 laparoscopic insufflation without trendelenburg, **10,11 and 12:** 12 mmHg of intraabdominal pressure and 5,10,15 degrees of trendelenburg position, **13:** 30 minutes after induction, **14:** 5 minutes after recovery of anaesthesia including reversal of curarisation.

After premedication (Midazolam), general anaesthesia was performed with Propofol, Alfentanyl, Atracurium, for maintaining heart rate less than 90 bpm and arterial Pressure <120/60mmHg. Ventilation was adjusted after endotracheal intubation in order to maintain PetCO2 at 35±3mmHg, particulary during insufflation.

At each time of the laparoscopy, 5 variables were collected : Intra Thoracic Pressure (ITP), Intraabdominal Pressure (IAP), End Tidal Carbon dioxid pressure (PetCO2), arterial oxygen saturation, by pulse oxymetry (SaO2) and degree of Trendelenburg (Trend). Statistical method was multivariate regression model, with stepwise procedure on SAS logiciel. $p<0,05$ on Fisher Test is statistically significant.

Results and discussion : Intraocular Pressure is not correlated with IAP ($p=0,4$) and SaO2 but with the degree of Trendelenburg Position ($p=0,007$) and intrathoracic Pressure $p<0,0001$. Interaction between Trendelenburg position and IAP and the 2 variables : ITP and PetCO2 has been tested and interaction Trend x PetCO2 influence IOP ($p=0,03$).

General anaesthesia and controlled ventilation maintaining low value of PetCO2 is known for reducing IOP (1,2). Trendelenburg Position increased IOP. Increase of ITP is due to Trendelenburg Position, to increase in intraabdominal pressure and to hyperventilation, necessary in order to maintain PetCO2 between 32 and 38mmHg. Increase in ITP is the most important variable influencing IOP.

Conclusion : Even though IOP values remains within normal range (15-20mmHg) (4) at each time of the laparoscopy, the Trendelenburg position, its effect on PetCO2, and increase in Intrathoracic pressure increases IOP, whereas IAP does not influence it. This could be due to increase in choroidal blood volume (3). In case of glaucoma, the proposed attitude is to measure IOP and reduce Trendelenburg position, ITP and PetCO2.

References : 1) Arch.Soc.Esp.Oftalmol., 49 : 1 : 49-55, 1985, 2) Glaucoma, 7 : 4 : 174-8, 1985, 3) Acta ophtalmol., 59/4 : 465-75, 1981, 4) EMC (Paris), 1-36620 E^{30} : 11, 1982

A.17

IN VIVO ASSESSMENT OF THE WORK OF BREATHING THROUGH DRY AND WET HEAT AND MOISTURE EXCHANGING DEVICES.

Quinn AC, Newman PJ, Allt-Graham J, Fawcett WJ.
St George's Hospital Medical School, London.

Heat and moisture exchanging (HME) devices are considered to be of low resistance and therefore should add little to the work of breathing (WOB). Although there is experimental data on WOB [1] through HMEs, there is no in vivo data. We have used a recently described technique of respiratory monitoring [2] to measure the in vivo WOB through HMEs in different conditions.

Five healthy volunteers were recruited. A 7 Fr gauge Bicore "smartcath" was inserted nasally under local anaesthesia into the lower oesophagus. The subject was blind to the test device and each device was placed distal to the pneumotachograph of the Bicore for two minutes. Four devices were tested:
1. Simple hygroscopic HME filter, Engstrom Edith.
2. Composite hygroscopic HME filter, Hygrobac S.
3. Hydrophobic pleated HME filter, Pall BB100.
4. Simple bacterial filter, the Filtaguard.

Filters were studied under 5 different conditions:
Baseline (B), dry (D), 6ml artificial saliva on patient side of the filter (S), 6ml water on ventilator side (W) and 6ml saliva on patient side + 6ml water on ventilator side (WS).
The mean and mean percentage change for WOB were calculated for each filter under each condition. Statistical analysis was by ANOVA on the mean values, followed by Scheffe's F test. A $p<0.05$ was taken as significant.

Four males and a female with a mean weight of 67 (range 55-76) kg, a mean age of 34 (range 28-48) years.

WOB (J/L)

	B	D	W	S	WS
Edith	0.59	0.59	0.66	0.81	0.80
Filtaguard	0.60	0.63	0.61	2.12*	2.06*
Hygrobac	0.62	0.71	1.38*	0.63	1.18
Pall	0.61	0.59	0.63	0.63	0.65

*$P< 0.01$ (within HME), and $P< 0.05$ (between HME, under same conditions)

Comparison between devices showed no differences when dry. The Pall and Edith devices showed no significant change in WOB under any of the conditions; the hydrobac and filtaguard caused significant increases as shown. This additional WOB may be of critical importance to the compromised spontaneously breathing patient.

References:
1. Chung R, Soni N. *Br J Anaesth* 1991; 67: 647P
2. Banner MJ et al. *Crit Care Med* 1992; 20: S68

A.18

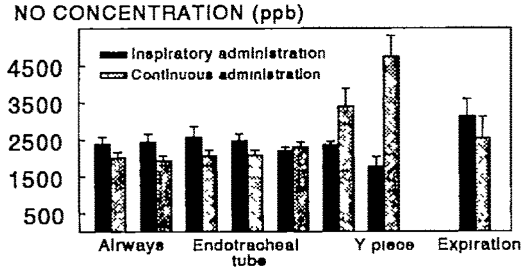
DISTRIBUTION OF NO CONCENTRATIONS DURING 2 METHODS OF NO INHALATION.

E. Mourgeon, L. Puybasset, M. H. Renaudin, C. Ravault, L. Bodin, J. J. Rouby, P. Viars.
Surgical Critical Care Unit, Department of Anesthesiology
Hopital de la Pitié, University of Paris VI, France

Continuous monitoring of inhaled NO concentrations using chemiluminescence is one of the safety guidelines for clinical use of NO in patients with ARDS. However, the most accurate site of measurement is still debated. The aim of this study was to measure NO concentrations at various sites of airways and respiratory circuits during 2 methods of NO administration in mechanically ventilated patients with ARDS.

Patients and methods. Seven patients (mean age 50 ± 9 yrs) with ARDS were prospectively studied after informed consent and institutional approval had been obtained. NO, released from a tank of nitrogen with a NO concentration of 2235 ppm (Air Liquid, France) was administered within the inspiratory limb of the ventilator either continuously at a flow rate of 30 ml/min or exclusively during mechanical insufflation of the ventilator using a specially constructed injection system (CFPO) connected to the nebulizer of the ventilator. Inhaled NO concentrations were measured using a bedside chemiluminescence apparatus (NOS 2000, Séres, France, aspiration flow rate - 150 ml/min) at different sites : within the tracheobronchial tree (5 and 10 cm from the distal tip of the endotracheal tube) and within respiratory circuits (6 sites of sampling located between the endotracheal tube and the end of the expiratory limb).

Results : As shown in the figure, inhaled NO concentrations were not different into airways, endotracheal tube and expiratory limb during both modes of administration. With continuous administration, a marked increase in NO concentration was found into the Y piece, near the site of injection.



Conclusion : Inhaled NO concentrations within the endotracheal tube are very close to tracheobronchial concentrations. The endotracheal tube appears an easy and reliable site where NO concentrations can be monitored in both method of administration.

A.19

Title : **RESONANT VOLUME AMPLIFICATION DURING HIGH FREQUENCY JET VENTILATION IN HUMAN**

Authors : J.L. BOURGAIN, V. BILLARD, E. DESRUENNES

Affiliation : Département d'Anesthésie Analgésie Réanimation, Institut Gustave-Roussy, 94800 Villejuif, France

Resonant tidal volume amplification (RVA) during high frequency ventilation has been previously reported in animals and in one study including a small number of patients (1). The aim of this study was to evaluate the RVA by spectral analysis of thoracic (RC) and abdominal (AB) displacements during high frequency jet ventilation (HFJV).

Methods : After informed consent, 74 patients scheduled for direct laryngoscopy were included. After induction (propofol alfentanil and vecuronium), patients were intubated and HFJV started (driving pressure 3.5bars, I: T ratio 35%, FiO_2: 1). Anaesthesia was maintained by a continuous infusion of propofol and intermittent reinjection of vecuronium according to train of four monitoring. RC and AB displacements were measured by two mercury strain gauges strapped to the thorax and the abdomen. Calibrations were performed in static condition using a 1000 ml syringe. For five respiratory rates (1, 2, 3, 4, 5Hz), signals were recorded to obtain the peak to peak displacement (Vt) (n=74) and processed by a real time spectral analyser (n=22) to obtain the amplitude of the two first harmonics (H_1 and H_2). Results are expressed in litres per minute by multiplying the displacements of each compartment by the calibration factor and the respiratory rate (RR) to obtain the minute ventilation (VAB and VRC).

Results : In spite of large individual variations, the increase in RC displacement at 4 and 5Hz was associated with an increased H_2 amplitude and the increase in AB displacement at 3Hz was associated with an increased H_1 amplitude. Same amplifications have been reported in similar conditions but in a lung model (2).

Conclusion : Although phase measurements were not available, resonant amplification is the more likely explanation to the increase in VRC above 3Hz.

RR (Hz)	1	2	3	4	5
V RC	13.1 (3.4)	13.9 (3.8)	13.9 (3.9)	19.2* (6.6)	19.8* (6.4)
H_1 RC	10.0 (3.1)	10.0 (3.4)	8.7 (3.9)	12.5 (6.0)	11.3 (5.4)
H_2 RC	2.2 (0.9)	3.5 (2.1)	3.2 (2.1)	7.8* (6.2)	8.9* (7.4)
V AB	10.8 (3.1)	12.2 (3.7)	15.6* (5.4)	15.1* (5.3)	12.0 (4.9)
H1 AB	8.7 (2.5)	10.4 (3.4)	14.3* (4.9)	12.4 (4.1)	8.7 (4.3)
H2 AB	2.4 (0.7)	3.2 (1.1)	2.6 (1.2)	1.9 (1.5)	1.8 (1.8)

*$p < 0.05$ ANOVA mean ± SD

References :

1) Crit Care Med 1990, 18, 1102-1106.
2) CR Acad Sci 1990, 310, 133-138.

A.20

Preoperative Checking of the Anaesthetic Machine
A Survey in a University Department of Anaesthesiology

C.E. Klopfenstein (1), M. Bernstein (2), E. Van Gessel, A. Forster (1)

Department of Anaesthesiology (1), Department of Medicine, Unit of Epidemiology (2)
University Hospital, Geneva, Switzerland

Background and goal of the study: Failure to check equipment is often considered as one of the factors associated with critical incidents in anaesthesia (1,2,3). It is not easy to understand why highly trained anaesthetists who are skilled and motivated fail to check equipment. The purpose of our study was to determine with a questionnaire the level of knowledge of staff physicians, residents in training and nurses regarding the checking of their anaesthetic machine.

Material and methods: 130 anonymous questionnaires concerning 13 different items based on the current check-lists of other countries were sent to 63 anaesthetic nurses, 33 staff-physicians and 34 residents in training of our institution. For every question, there were 4 possible reponses (*never - seldom - often - always*) rated from 0 to 3. Seven snare-questions were inserted. All scores are expressed as mean±SD and were analysed using analysis of variance or chi-square as required.

Results: The overall response rate was 75% (98/130), subdivided into 30/33 staff, 23/34 residents and 45/63 nurses (p<0.05 for staff vs residents and nurses). Table 1 shows the results of both regular and snare questions, as well as mean scores for the 6 most representative items.

Discussion and conclusions: In our questionnaire, nurses have a higher total score than doctors. However, gas cylinders are too rarely checked by all participants. Oxygen-analysers as well as disconnection-alarms are not often enough checked by doctors, which could mean that they are less aware of the importance of these items. Circles and suction are the only items always checked by all participants.

Though it appears that nurses check the anaesthetic machine more thoroughly than doctors; this finding should be analysed with caution, since the nurses also have a higher global score for the snare questions.

References: 1. Craig et al, Anaesthesia, 1981; 2. Cooper et al, Anesthesiology; 1984; 3. Chopra et al, Br. J. Anaesth, 1992

Table 1. Mean ± SD of scores comparing 3 groups of anaesthetists

	mean total score (true question)	mean total-score (snare-questions)	Gas cylinders	Gas pipe-lines	Breathing system (circle)	O2-analyser	Disconnection alarm	Suction
staff-physicians (n = 30)	2.01 ±0.66	1.56 ±0.71	1.35 ±0.33	2.33 ±0.46	2.69 ±0.20	1.89 ±0.49	2.02 ±0.71	2.72 ±0.21
residents in training (n = 23)	2.05 ±0.70	1.76 ±0.62	1.10 ±0.44	2.24 ±0.21	2.79 ±0.10	2.08 ±0.81	2.02 ±0.58	2.81 ±0.18
nurses (n = 45)	2.35 ±0.56	1.89 ±0.32	1.62 ±0.22	2.31 0.74	2.93 ±0.04	2.32 ±0.04	2.42 ±0.54	2.83 ±0.14

* p < 0.05 ; score rating: 0 = never; 3 = always

A.21

IMPROVEMENT OF STRESS TOLERANCE IN ANESTHESIOLOGISTS BY CARDIOVASCULAR FITNESS TRAINING

C. Traunmüller, C. Weinstabl, M.D.,
R. Fitzgerald, M.D., A. Anvari, M.D.,
A.F. Hammerle, M.D.
Dept. of Anesthesiology, University of Vienna, 1090 Vienna, Austria.

The aim of several studies in the field of work-related stress management is to improve stress tolerance during daily routine and specific stress situations. We developed a new approach using individual physical training to improve stress tolerance in anesthesiologists.

Methods: The study was performed in 20 staff anesthesiologists (mean age 31 years, range 25-35 years) of either sex in a Level I trauma department. None of them performed regular physical training before entering the study. Prior to the study an estimation of body fat distribution (Futrex 5000™) and a Conconi-test (1) for determination of the anaerobic treshold was done. Following the check-up a 24 hours ECG monitoring was recorded in all volunteers during day and night duty. Anesthesiologists were allocated in group I (3 months lasting individual computer-based fitness-training) and group II (served as a control without training). Body fat (BF), heart rate (HR), 24 hours ECG monitoring and Conconi-test (CT) were repeated three months later during a comparable day and night duty in all volunteers. Mental disposition of all anesthesiologists was determined prior to and following the study period according to an evaluation scale of Zerssen (2). For statistical evaluation Student's t-test was done. A p value < 0.05 was considered significant.

Results: Data (mean±SD) of both groups are shown in the following table.

	GROUP I pre training	GROUP I post training	GROUP II without training	GROUP II without training
HR	80±7	72±7*	82±7	83±10
BF %	26±5	18±4*	28±8	29±6
CT	176±10 10±1	176±6 13±1*	180±9 9±3	181±10 9±10

CT is expressed as HR/km/h; * p<0.05

Mental disposition did not change in both groups.

Discussion: The results of our study show, that an improvement of the physical status (decrease of BF and increase of the anaerobic treshold) leads to a better tolerance of work related stress in anesthesiologists enrolled in the management of high risk patients. In emergency situations, HR as the gold standard in stress studies (3) was significantly reduced concerning stress response, based on significantly lower mean HR over 24 hours, in group I with regular exercise. Despite better work related stress tolerance, improvement of physical condition does not have an impact on mental disposition.

We conclude, that the results of our study stresses the need of regular physical training in anesthesiologists.

1. J Appl Physiol 52: 869-873, 1982.
2. Psychological Measurements in Psychopharmacology. Modern Problems of Pharmacopsychiatry 7: 189-202, 1974.
3. Anaesthesist 26: 375-380; 1977.

A.22

COMPARISON OF CEMENTED vs NON-CEMENTED TOTAL HIP IMPLANTS ON CARDIOPULMONARY FUNCTION

G.ZAOUK ^{1},E.GILBART^1, Ph.LEJEUNE^2, S.ELBANNA^3, E.BALATONI^1.
Departments of Anaesthesia^1, Intensive Care^2 and Orthopaedic Surgery^3
Hospital VESALE, MONTIGNY-le-TILLEUL, BELGIUM

Background and goal of the study:
This study was conducted to compare the effects of cemented or non-cemented implants during total hip replacement surgery on cardiorespiratory physiology and to ascertain whether methylmethacrylate (MMA) played an eventual role in haemodynamic variations.

Methods:
After hospital Ethics Committee approval and patient informed consent, 20 patients (ASA I-II, 68±11 years, 11M/9F), scheduled for total hip surgery, were randomized into 2 groups to receive either a cemented implant (group A, N=10) or a non-cemented one (group B, N=10). Continuous monitoring of mixed venous oxygen saturation (SvO2 - Oximetrics*) and radial arterial oxygen partial pressure (PaO2 - Continucath*) were placed prior induction of general anaesthesia, as well as EKG, pulse-oximetry and capnography.

Results and discussion :
The 2 groups were comparable in age, sex ratio, blood loss, diuresis, fluid and blood replacement, duration of surgery and anaesthesia and there was no clinical pulmonary embolism noted.

Analysis of variance showed no statistical difference between the 2 groups concerning SvO2 trend (Fig.1), PaO2 trend, haemodynamic data , gasometric measurements or calculated values.

So we conclude that, in our study, there was no evidence that MMA (group A) was responsible for any perioperative cardiopulmonary change.

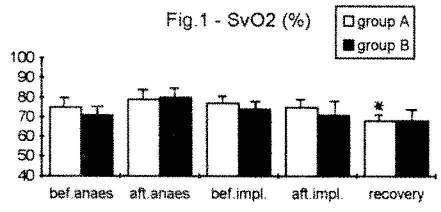


Fig.1 - SvO2 (%)

*p<0.05 vs previous value (Neuman-Keul test)

A.23

EMBOLISM DETECTED BY TEE DURING CEMENTED TOTAL HIP ARTHROPLASTY

Noëlle D. Lafont, MD,Willy M. Kostucki, MD,
Jean G. Boogaerts, MD, PhD.

Department of Anaesthesiology and Intensive Care, Reine Fabiola Hospital, Montignies/Sambre, Belgium.

Background: Bone cement implantation during total hip arthroplasty (THA) has been associated with venous embolism detected with transesophageal echocardiography (TEE)(1). We observed 15 patients scheduled for THA. We report a case illustrating a huge amount of echogenic material that was embolized into the right heart and partially entrapped in the pulmonary artery, as detected by TEE.

Patients and methods: A 76 year old woman ASA II was scheduled for THA. Anaesthesia was maintained with titrated halothane in a mixture of 50% O2:5O% N2O, associated with booster injections of fentanyl. Intraoperative monitoring included : heart rate, pulse oxymetry, PetCO$_2$, arterial and venous central pressures , blood gases and TEE. During the placement of the acetabular component, a "snow flurry" picture was recorded and followed by several highly echogenic and mobile emboli of various sizes (from 5 to 10 mm in diameter, some of them with a worm shape of 1 to 5 cm long) detected in the right atrium(Fig). At the time of the femoral component and during relocation of the hip joint , the same sequence of events was observed. At skin closure, the probe was positionned to visualize the pulmonary artery bifurcation. An echogenic material was found in the right branch of the pulmonary artery adherent to the vascular wall. No change was observed in any of the hemodynamic variables. The patient fared quite well after the operation. A pulmonary radionuclide study performed the first day after the operation was normal.

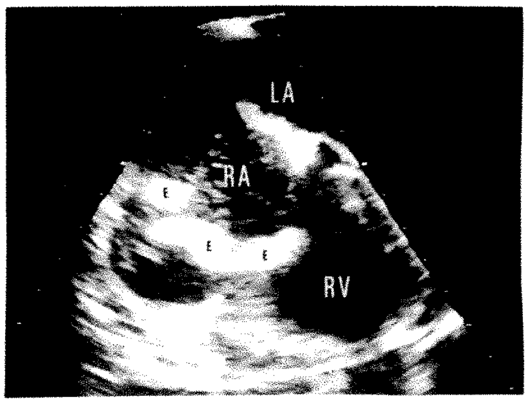


Figure.RA:right atrium,LA:left atrium,RV:right ventr,E:embol

Discussion: This case confirms the absence of correlation beetween echocardiographic views of venous emboli and hemodynamic and gazometric variables (1). The emboli were well tolerated by the patient, despite their volumetric importance. The correct nature of the embolic material cannot be stated by ultrasons but the worm shape of type A of the highly echogenic material is compatible with a peripheral venous moulded formation (2). This material can migrate into the pulmonary tree. Why this embolization does not cause hemodynamic modifications, gazometric changes and radionuclide mismatch remains an unsolved question.

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A.24

ANYBODY CAN DETECT MINIMAL CO2 EMBOLISM WITH A TRANSESOPHAGEAL DOPPLER MONITOR

T. Gillart, J.E. Bazin, M. Aubert,
P. Schoeffler

**Departement d'anesthesie. CHU. 63003
Clermont-Ferrand France.**

Background and goal of study: Carbon dioxide embolism is a rare complication of laparoscopy which can be lethal. The best treatment remaining immediate discontinuation of insufflation when small bubbles are detected, the necessity of carefully monitoring the patients for early diagnosis and treatment appears to be important. This study was designed to test the sensitivity of transesophageal doppler sound when heard by unskilled population.

Materials and methods: An anesthetized pig weighing 21 Kg and scheduled for laparoscopic surgery training (intraperitoneal pressure obtained being 12mmHg) was monitored for venous gas embolism with transoesophageal doppler (ODM1 Abbott). The Doppler ultrasound flow transducer was placed at the level of inferior vena cava, the correct position being assessed by intensity and quality variations of sound with ventilation. Twelve injections of 0,1/0,05 /0,025 and 0,01 ml of CO2 were made in a random sequence via a femoral venous catheter (Seldicath 1 mm). An unmistakable audible change in frequency on doppler ultrasound could be noted immediately (delay < 2s) by the authors after each injection, and recorded well in an audio tape.

Forty uninitiated people (10 medical students, 12 nurses, 6 nurse-assistants, 5 secretaries, 8 children, 7 to 15 years old) were requested to listen individually to the tape recording.

Results and discussion: All Doppler changes were detected by every listener. Only Four people noted one or two additionnal sounds. The sensitivity of 100% appears to be unchanged when used by experienced or inexperienced operators, as little gas volume as 0,01ml included.Specificity remains very good in the surgical environment where interferences may occur.

Conclusion: According to previous studies (1,2), transoesophageal Doppler is a good procedure for detecting minimal gas embolism during laparoscopy. This device can be utilized in the operating theater with minimal preparation by an unexperimented personnel.

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A.25

Doppler-guided puncture of the axillary vein in ICU-patients

Werner Schregel, Heike Hoer, Marian Sihle-Wissel,
Günter Cunitz

Klinik für Anaesthesie und operative Intensivtherapie,
Knappschaftskrankenhaus, Ruhr-Universität Bochum
(RUB)

Background and goal of study: Puncture of the axillary vein was claimed to be a safe central venous access (1). However, anatomical "landmarks" recommended for vein location (e. g. M. pectoralis minor) are hard to find in many intensive care patients. This investigation should evaluate unidirectional Doppler-ultrasound for locating the axillary vein.

Methods: According to the experimentel design approved by the local Ethical Committee (RUB) 50 cannulations of the axillary vein were attempted in patients of our intensive care unit. Patients were placed in a 15° head-down-position, the arm was abducted to 45° (1). The axillary vein was located by Doppler ultrasound and marked on the skin with a felt pen. Ultrasound intensity was judged by a score ranging from 0 to 4. After skin desinfection, sterile draping and local anaesthesia, puncture was attempted with the needle of the puncture system (Leader-Cath 11515, Vygon, Aachen, FRG). If venous blood could be aspirated, the Seldinger guide wire was inserted and the definite catheter placed. The puncture attempts were evaluated in respect to success rates, time, ultrasound intensity, complications and malposition.

Results and discussion: 43 of the attempted 50 central venous catheters were placed successful. In two cases, axillary vein was not hit by the puncture needle. Guide wire placement did not succeed in four patients. One catheter was malpositioned in the ipsilateral internal jugular vein. Four inadvertent punctures of the axillary artery remained without sequelae after compression. No further puncture related complications were observed. With high ultrasound intensity, the number of puncture attempts necessary for successful vein cannulation was lower. Complications and puncture failure seemed to be more frequent in patients with low ultrasound intensity score. Axillary vein location by Doppler ultrasound is likely to improve cannulation results and to reduce complications induced by "blind" needle probing.

Conclusion: Central venous access via the axillary vein had a satisfying success rate (43/50) and proved to be safe in our patients with several risk factors for the development of complications. Doppler-guided puncture of the axillary vein seems to be a promising central venous access, for example in patients with extended tumor operations involving head and neck.

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A.26

CENTRAL VENOUS CATHETER PLACEMENT USING THE CAVAFIX-CERTODYN SD CATHETER

Stijn A. Corsten; Boudewijn van Dijk; Niels C. Bakker; Gert J. Scheffer; Jaap J. de Lange

Department of Anaesthesiology, Free University Hospital, Amsterdam, The Netherlands

Background & goal of the study: Malposition of central venous catheters occurs in 3-38% of the insertions (1). Confirmation of a correct position of the cathetertip before use of the catheter and during the sterile insertion procedure is recommended (2). Positioning of the central venous catheter by an ECG-derived signal from the catheter is an interesting option peri-operatively and in emergency-situations. This method is reported by various authors but became not commonly wide-spread. In the new Cavafix-Certodyn SD catheter (B.Braun AG, Melsungen, Germany) the ECG signal from the cathetertip is conducted by an intraluminal wire in stead of an electrolyte solution. This might lead to a better conductance and a less distorted signal.

The purpose of this study was to evaluate this catheter in clinical use and to determine if correct positioning of the cathetertip in the superior caval vein by an ECG-signal could replace radiologic control.

Materials and methods: In 89 elective and emergency surgical patients requiring central venous catheterization peroperatively a catheter was inserted from various insertion sites. Discrimination of an atrial position of the cathetertip (p-atriale) was followed by a 3 centimetres withdrawal of the catheter into the superior caval vein. Postoperative comparison with a chest X-ray was made by a radiologist, who was not aware of the ECG-registration.

Results and discussion: In 81 patients (91%) with discrimination of a p-atriale and appearance of an normal p-wave after 3 centimetres withdrawal of the catheter the tip was located in the superior caval vein at the chest X-ray. In 7 of the 8 patients without a p-atriale discrimination the cathetertip was located at an aberrant position.

Conclusions: The wire conducted intravascular ECG signal is a useful tool for positioning a central venous catheter. The Cavafix Certodyn SD technique proved to be an easy and reliable method. It is our opinion that uncomplicated insertions from several insertion sites do not require radiologic examination for the control of the cathetertip position. If during the insertion of the catheter no p-atriale can be seen, an aberrant position of the catheter tip is almost certain.

References:

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A.27

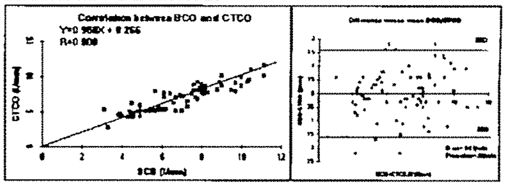
EVALUATION OF CONTINUOUS CARDIAC OUTPUT MONITORING WITH A NEW PULMONARY ARTERY CATHETER

Catoire P, Orliaguet G, Beydon L, Liu N, Bonnet F,
Réanimation Chirurgicale, Hôpital Henri Mondor,
94010 Créteil, France

Background and goal of the study: A new continuous thermodilution cardiac output (CTCO) catheter has been introduced recently. Reliability of this catheter has been determined by comparison to intermittent CO bolus measurements with thermodilution (BCO), at fixed intervals (1). Rapid changes in hemodynamic condition may occur in ICU patients, not documented by predetermined measurements. We therefore examined how accurately CTCO measurements accounted for the changes in CO in a double-blind prospective study.

Materials and Methods : A CTCO catheter (Intellicath TM -Baxter), connected to a monitor (Vigilance^{TM}-Baxter), was inserted in 10 ICU patients requiring invasive hemodynamic assessment. CTCO measurements were blinded to the physician in charge of the patient but were initially alarmed within a 1l/min range around the value corresponding to a stable hemo-dynamic status for a given patient. When required by the patient's condition or when the CTCO monitor alarmed, the physician performed a BCO measurement. The time necessary to obtain the BCO (as the mean of 4 measurements) was recorded. The mean value itself was compared later on with CTCO measurements. Comparisons were achieved by linear regression and according to the Bland and Altman method.

Results and Discussion:



Eighty-one data sets were obtained.The reproducibility of two measurements of CTCO was 3% versus 20% with BCO.The precision of CTCO was .8 l/min (13%). CTCO measurements allowed to save 5±2 minutes and pointed out an hemodynamic problem not diagnosed by the physician in charge, in 19 cases.

Conclusion: The precision of CTCO equals the reproducibility of BCO previously determined (2). CTCO appears as a usefull monitoring technique in patients with unstable hemodynamic condition.

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2/ Stetz CW: Reliability of the thermodilution method in the determination of cardiac output in clinical practice. Am. Rev. of Respir. Dis. 1982; 126: 1001-1004

A.28

Clinical evaluation of continuous cardiac output monitoring in cardiac surgical patients

B.W. Böttiger , M. Soder, F. Fleischer,
H. Böhrer, J. Motsch, E. Martin

Department of Anaesthesia, University of Heidelberg,
D-69120 Heidelberg, Germany

Background: Continuous cardiac output (CCO) measurements may be based on the thermodilution technique using a thermal filament mounted on a Swan-Ganz catheter (Vigilance™, Baxter Healthcare Corp., Irvine CA)[1,2]. With the same catheter, standard injectate cardiac output (ICO) values may be obtained. The aim of our study was to evaluate the correlation between ICO and CCO measurements in patients undergoing coronary artery bypass grafting.

Materials and methods: After institutional approval and informed consent, 25 patients undergoing coronary revascularisation were cannulated under local anaesthesia. Cardiac output measurements were taken prior to (T_1) and immediately after induction (T_2) of anaesthesia, before sternotomy (T_3), 5 min later (T_4), and after heparin administration (T_5). Hypothermic low-flow, low-pressure perfusion was used as extracorporeal circulation (ECC) technique. A further set of measurements was obtained after weaning from ECC: after 5 min (T_6), 15 min (T_7), 30 min (T_8), 45 min (T_9), 1 h (T_{10}), 90 min (T_{11}), 2 hrs (T_{12}), 3 hrs (T_{13}), 4 hrs (T_{14}), 6 hrs (T_{15}), 8 hrs (T_{16}), 10 hrs (T_{17}), and after 12 hrs (T_{18}). ICO measurements were made in triplicate at end-expiration using boluses of cold saline solution. The mean value was recorded as ICO. CCO measurements were taken simultaneously. Blood and rectal temperatures were measured at all time points. Correlation coefficients (r) were calculated and statistical evaluation was performed using correlation coefficient analysis (Pearson) for every time point.

Results: Cardiac output measurements yielded 450 data sets. A high positive correlation ($p<0.01$) between ICO and CCO was detected at T_{1-5} and T_{10-18} (fig. 1). Little correlation was found at T_{8-9}.

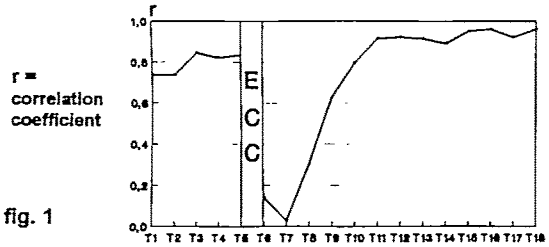

fig. 1

Discussion: Our results show a significant positive correlation between CCO and standard ICO measure-ments before ECC and more than 45 min after ECC. In the initial phase following ECC, there is no correlation between CCO and ICO. Further investigation is needed to clarify whether rapid changes in blood temperature during this rewarming period account for this finding.

References: 1. Lichtenthal PR et al: Crit Care Med 1993;21: S214; 2. Yelderman ML et al: J Cardiothor Vasc Anesth 1992;6:270-274.

A.29

DETERMINATION OF CARDIAC OUTPUT AT DIFFERENT VENTILATORY CONDITIONS - COMPARISON OF BIOIMPEDANCE WITH THERMODILUTION

P. Altmayer, J. Helms, P. Welsch, U. Grundmann

Klinik für Anaesthesiologie und Intensivmedizin, Universität des Saarlandes, D-66421 Homburg/Saar, Germany

Background: The determination of cardiac output with the noninvasive thoracic electrical bioimpedance methode (TEB) is well established, and a good correlation with the thermodilution technique (TD) has been shown. In animal studies under the condition of artificial ventilation cardiac output measurements with TD showed a considerable variability depending on the measuring point within the respiratory cycle. In the present study the effects of different standardized conditions during mechanical ventilation on the accuracy of TEB compared to TD were evaluated in patients.

Material and methods: After obtaining institutional approval and informed consent the study was performed in 12 patients (ASA II-III) undergoing neurosurgical surgery of intracranial tumors or aneurysms. For monitoring cardiac output a TEB device (BoMed, NCCOM3-R7) and TD computer (Edwards, model 9520) was used. The patients were ventilated with $N_2O:O_2$ (1:1), the minute ventilation was in all cases 100 ml/kg (Dräger, AV-1). In general anaesthesia with midazolam/alfentanil under stable hemodynamic conditions simultaneous measurements of cardiac output were performed at different ventilatory states: 1. fixed points of the ventilatory cycle (at the first third of inspiration and in endexpiratory apnea) and 2. spread over the entire ventilatory cycle with low respiratory rate (8/min) and high tidal volume (here with and without PEEP of 8 cm H_2O) and with a higher respiratory rate (16/min) and low tidal volume. The calculations were based on a total of 1168 simultaneous measurements.

Results and discussion: Both methods correlated under all conditions with a mean difference of 0.85% (Range from -3.1% to 6.5% for the subgroups). The best agreement was found in endexpiratory apnea. Under these conditions the relative differences between the measurements with the two methods showed an equal distribution with a bias of -3.1%. For the other subgroups the TEB overestimated the cardiac output slightly at lower values, in particular during PEEP conditions.

Conclusion: TEB provides a noninvasive and reliable method for measuring cardiac output. Even under the most different conditions of artificial ventilation a sufficient correlation with the standard TD could be seen.

A.30

THE ACCURACY OF IMPEDANCE CARDIOGRAPHY IN MEASUREMENT OF CARDIAC OUTPUT IN COMPARISON WITH THERMODILUTION METHOD

KAR-LOK WONG, MD.

Dept. of Anesthesia, Mackay Memorial Hospital,
Taipei, Taiwan
Dept. of Anesthesiology, Taipei Medical College,
Taipei, Taiwan, R.O.C.

Introduction

Continuous noninvasive measurement of cardiac output (CO) is clinically desirable. Thoracic electrical bioimpedance (TEB) is a noninvasive technique which measures stroke volume on a beat-by-beat basis. It was originally developed for use by the U.S. astronauts during the late 1960s and early 1970s. However only in the last few years have satisfactory results been obtained, primarily because of improved technology and a refined mathematical equation encoded in the microprocessor of a commercially available digital computer. The purpose of this study was to compare the accuracy of TEB (NCCOM3-R7, BoMed Medical Manufacturing Ltd., Irvine, CA) with the thermodilution (TD) method of measuring CO during surgery.

Methods

Eighteen patients (age 39-64 yr), with coronary artery disease undergoing coronary artery bypass graft surgery were studied. Patients were excluded if severe dysrhythmias or aortic insufficiency was present preoperatively. Simultaneous measurements of CO were performed in each patient with the use of a 7FSwan-Ganz catheter and TEB. 128 matched pair values were obtained and analyzed by Linear regression analysis and Student's t-test.

Results

A good correlation (correlation coefficient $r=0.86$, $TEB=0.55+0.82\ TD$) between the two methods of cardiac output measurements was resulted. The Student's t-test demonstrated that the correlation between TEB and TD was statistically significant ($p < 0.05$).

Discussion

In conclusion, technological advances in TEB have resulted in more accurate CO measurements. Such device offers a noninvasive alternative to the TD technique for the determination of CO, and may potentially be very useful as a powerful, noninvasive, continuous technique for monitoring cardiac function in the clinical setting.

A.31

HEMODYNAMIC EFFECTS OF LAPAROSCOPIC CHOLECYSTECTOMY IN PATIENTS WITH CORONARY DISEASE

C. Duale, JE Bazin, C. Ferrier, F. Ruiz, P. Schoeffler.

Department of Anesthesiology, CHU,
63003 Clermont-Ferrand, France.

Background and goal of study: Laparoscopic cholecystectomy has emerged as the favored technique because of the shorter recovery time, but no data are available concerning this procedure in patients with coronary disease. The aim of this study was to investigate the hemodynamic variations during laparoscopic cholecystectomy in these patients.

Materials and methods: With approval of our institution's ethics committee and with their informed consent, 11 patients with documented coronary disease (ASA III-IV), scheduled for elective laparoscopic cholecystectomy, were included in this study. After premedication with oral hydroxyzine (75 mg 1 hour before surgery), general anaesthesia was induced with etomidate (0,2 mg/kg), fentanyl (2 µg/kg) and atracurium (0,5 mg/kg) followed by maintenance with 50 % nitrous oxide in oxygen and fentanyl (2 µg/kg/h). Minute ventilation was adjusted in order to maintain $PETCO_2$ between 32 and 35 mmHg. Intra-abdominal pressure did not exceed 12 mmHg. Hemodynamic parameters were obtained from a 7 F Swan-Ganz thermodilution catheter and from radial artery canulation.

In all patients, isoflurane (0,5-1,5 %) was used in order to prevent the increase in systemic vascular resistances after abdominal insufflation. In 3 cases, this vasodilatation was completed using nicardipine (2-3 mg/h). One patient, with a cardiac index below 1.5 l/min/m^2, despite a high capillary wedge pressure, required an inotropic support (dopamine 10 µg/kg/min).

Hemodynamic parameters were recorded 10 min after induction (T1), 5 min after the peritoneal insufflation (T2), 5 min after tilting to 15° head-up position (T3), 30 min later in the same conditions (T4), and 10 min after exsufflation (T5). Data expressed as mean were analyzed by ANOVA and Kruskal-Wallis' test. Values of $p < 0.05$ were considered significant.

Results and discussion:

	T1	T2	T3	T4	T5
HR (Bt/min)	58.7	63.8	68.7	63.4	70
MAP (mmHg)	90.9	99.8	102	98.6	96.4
CI (l/min/m^2)	1.68	1.91	2.28	2.35	2.99*
SVR (dyn/s/cm^5)	4215	3703	3491	2906	2582

*: $p < 0.05$

Peritoneal insufflation during laparoscopy is known to increase systemic vascular resistances and to decrease cardiac output [1]. In this study the administration of isoflurane (completed by nicardipine in 3 cases) corrected theses adverse hemodynamic effects. These data suggest the usefulness of isoflurane and nicardipine during laparoscopic cholecystectomy in patients with coronary disease. More information is required for very long-lasting procedures, such as laparoscopic colectomy or hysterectomy, with special attention to regional circulations in these patients.

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A.32

HAEMODYNAMIC CHANGES DURING LAPAROSCOPIC CHOLECYSTECTOMY IN THE ELDERLY (preliminary results).

Karin Dhoste, Jérome Karayan, Louis Lacoste, M.Suzanne Lehuedé, Jacques Fusciardi.

Departments of Anaesthesiology, Surgery and Pharmacy, Jean Bernard Hospital and University School of Medicine, 86021 Poitiers, France.

Background and goal of study: Old patients are been easily referred to cholecystectomy since the development of the laparoscopic technique. The aim of this study was to investigate the pneumoperitoneum induced haemodynamic changes in patients>75 years and ASA III physical status.

Materials and methods: 10 patients (80±3years) scheduled for laparoscopic cholecystectomy were included in this prospective study. Usual cardiovascular treatment and hydroxyzine (1mg. kg-1) were administered 2 hours before surgery. The cardiovascular monitoring included : ECG, continuous radial arterial pressure and a Swan-Ganz catheter (Baxter RE-FOX*)for mesurements of S$\bar{v}$O2,CO,RVEF and calculation of RVTDVI. Measurements were performed before(T1) and 10min after (T2) anaesthetic induction, then 15min(T3), 30min(T4), 60min(T5) after the beginning of insufflation in a 10° head up position, and 15min after exsufflation(T6). Anaesthesia used fentanyl(3mcg.kg-1), etomidate(0.3mg. kg-1) and atracurium for tracheal intubation. Ventilation was controlled(PETCO2:30-40mmHg) and used N2O:O2=50%.Anaesthesia was maintained with isoflurane and fentanyl as needed. The duration of the pneumoperitoneum was 81±16 min with a 12mmHg automatically regulated intra abdominal pressure (IAP). Data (mean±SD) were statistically analyzed with ANOVA (p<0.05).

Results and conclusion: Haemodynamics is summarized in the table. The maximum cardiovascular depression was recorded after induction of anaesthesia. IAP and surgery resulted in an improvement in MAP,CI and S$\bar{v}$O2. Neither RVTDVI nor RVEF indicates an improvement in cardiac preload or cardiac function. A sympathetic stimulation caused by surgery and/or increases in PCO2 is suggested. In conclusion a pneumoperitoneum of 81 min duration with IAP=12mmHg, as well as exsufflation, seem hemodynamically well tolerated by the elderly.

Table: Haemodynamic changes during laparoscopic cholecystectomy in the elderly.

	T1	T2	T3	T4	T5	T6
MAP mmHg	112±11	85±13*	104±22°	98±8*°	89±12*	92±16*
HR beats/min	70±7	58±6*	67±13°	70±11°	67±12°	68±15°
CI L/min/m2	2.6±0.4	1.5±0.4*	2±0.5*°	2±0.4*°	2±0.5*°	2±0.6*°
S$\bar{v}$O2 %	74±2	76±3	80±3*	78±4	81±2*°	80±6*
RVEF %	40±4	32±5*	35±6	35±5*	36±8	33±6*
RVTDVI ml/beats/m2	94±13	82±16	83±10	89±19	86±23	92±8
PETCO2 mmHg		28±3	32±3	33±3°	36±7°	32±8°

* P<0.05 vs T1, ° P<0.05 vs T2

A.33

HEMODYNAMIC CHANGES DURING LAPARASCOPY.

K. Myre* G. Smith**T.Buanes***and O. Stokland*
Dept. of Anaesthesia* Cardiology** and Surgery***
Ullevaal Hospital, Oslo, Norway

Laparascopic diagnosis and surgery assume expansion of the abdominal cavity by gas. Intraabdominal pressure by 12 - 15 mmHg increases arterial pressure, but other hemodynamic data are not fully elucidated - even in patients without cardiac disease. We have therefore recorded hemodynamic changes in 12 patients without cardiac disease according to a protocol approved by the regional ethical comittee and after oral and written information and consent from the patient.

METHODS: During general anesthesia (midazolam,. fentanyl, thiopental, pancuronium and isoflurane) a Swan-Ganz catheter was introduced into the internal jugular vein and advanced into the pulmonary artery. The radial artery was cannulated. All patients were ventillated by a volume cycled respirator and monitored by ECG, pulsoxymetry and capnography in addition to venous and arterial blood pressures recordings. In the last 5 patients we simultaneously also measured heart volume by transoesophageal echocardiography (TEE). Carbone dioxide was insufflated into the abdominal cavity to maintain a constant pressure of 15mmHg.

RESULTS:

	MAP	mPAP	PCWP	HR	CI	SVRI	PVRI
Before insufflation	71.2 ±8.6	16.0 ±2.2	9.6 ±1.9	63.6 ±11.6	2.1 ±0.4	2473 ±578	262 ±110
During insufflation	100.6 ±8.9	24.5 ±3.5	18.5 ±1.9	64.3 ±11.2	2.0 ±0.4	3563 ±739	292 ±97

MAP=mean arterial pressure, mPAP=mean pulmonary arterial pressure, PCW= pulmonary capillary wedge pressure, HR=heart rate, CI= cardiac index, SVRI=systemic vascular resistance index, PVRI=pulmonary vascular resistance index

DISCUSSION: Left ventricular diastolic pressure , jugded by PCWP,was doubled during the insufflation. MAP and SVRI both increase by about 40% and CI remains unchanged. From the data we could presume that the heart was dilated by the increase in PCWP. Laparascopy could therefore be risky in patiens with coronary ischemia.

However, intrathoracic pressure (judged by respiratory pressures) increased which changed the pressure- volume relationship in the left ventricle. The PCWP changes from control to intervention did therefore not reflect the changes in left ventricular volume. In the 5 last patients we therefore also measured left ventricular dimensions by TEE. Despite the increases in PCWP we did not find any increase in left ventricular volume.

CONCLUSION: **Insuflation of CO2 in the abdominal cavity to 15 mmHg doubles the PCWP, but does not increase left ventricular volume and CI. Because the left ventricle does not dilate despite the increase in PCWP the gas insufflation seems to be less risky than presumed. It remains to record simultaneous echo- and hemodynamic data in more patients.**

A.34

DIAPHRAGMATIC FUNCTION AFTER LAPAROSCOPIC CHOLECYSTECTOMY

R. Sharma, F. Clergue, E. Jansson, S. Reiz

From the Departments of Anaesthesia and Intensive Care, University of Umeå, Umeå, Sweden and CHU Tenon, Paris, France.

Background & goal of study: Changes in transdiaphragmatic pressure and rib cage versus abdominal diameters have suggested diaphragmatic dysfunction after open upper abdominal surgery (1). Similar information from upper laparoscopic surgery is lacking. This study evaluates diaphragmatic function after laparoscopic cholecystectomy (LC) using multiple indices for diaphragmatic dysfunction.

Materials & methods: Eight female ASA1 and ASA2 patients were subjected to LC under thiopental-fentanyl-vecuronium-nitrous oxide-isoflurane anaesthesia after diazepam premedication. Muscle relaxation was reversed at the end of surgery by neostigmine. Patients were studied in the supine position before premedication, and 1h, 6h and 24h postoperatively. Ketorolac and ketobemidone were used for pain relief. Gastric and oesophageal pressures (Pga & Poes) were recorded via a double lumen nasogastric tube. The contributions of thoracic (Vthor) and abdominal (Vabd) breathing to quiet breathing tidal volume (VT) were recorded by a Respitrace® system. EMG was recorded via a bipolar electrode inserted into the cupole of the right diaphragm. Respitrace® and presssure recordings were made before surgery and combined with the EMG at 1h, 6h and 24h after surgery. EMG data at 1h and 6h are given in % of the 24h amplitude/Ti (inspiratory time).

Results: Patients were fully awake without residual muscle relaxation 1h postoperatively. EMG was missing in 1/8 due to poor contact. 1/7 had no EMG activity at 1h. At 1h, and 6h, mean±SD EMG ampl/Ti was 40±25% and 67±22% of the 24 h value respectively ($p=0.002$ and $p=0.013$ compared to the 24h value). VT was significantly decreased at 6h (333±184 ml vs 429±142 ml at control, $p=0.041$). Konno-Mead plots (2) of Vthor vs Vabd demonstrated a shift towards thoracic breathing at 1h, 6 h and 24h (Vthor%/Vabd%: control - 20/80, 1h - 57/43, $p=0.014$, 6h - 50/50, $p=0.003$, 24h - 44/56, $p=0.002$). ΔPga/ΔPoes was positive in 6/8 at 1h, in 4/8 at 6h and in 0/8 at 24h.

Discussion and conclusion: Plots of ΔPga/ΔPoes, a shift from predominantly abdominal to rib cage breathing, and directly recorded EMG all document diaphragmatic dysfunction early after LC. The paradoxical movement of the diaphragm indicated by negative changes in gastric pressure and positive values for ΔPga/ΔPoes was progressively normalised within 24h along with an increase of the EMG amplitude/Ti. However, the presence of predominant rib cage breathing and minimal variations in ΔPga 24h after surgery suggest that diaphragmatic function had not been completely restored.

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A.35

CARDIO-RESPIRATORY & MUSCULAR CAPACITY AFTER LAPAROSCOPIC CHOLECYSTECTOMY

Delaunay L.*, Bonnet F.*, Rimaniol J.M.*, Cherqui D.+, Atlan G.++
*Réanimation chirurgicale, ++Service d'Explorations fonctionnelles ,+Service de chirurgie digestive.
Hôpital H. Mondor, 94010 Créteil.

Introduction : Many patients complain of postoperative fatigue after abdominal surgery associated with muscular weakness and cardiorespiratory changes (1) (2). Convalescence seems to be better after laparoscopic than after open cholecyctectomy (3). The aim of this study was to evaluate prospectively muscular and cardiorespiratory capacity during a submaximal exercise after laparoscopic surgery.

Patients and Methods : After informed consent 8 patients scheduled for laparoscopic cholecystectomy were studied. Anaesthesia and postoperative pain control were standardised. All patients were examined once preoperatively and on the 3rd and 10th postoperative days. Subjective feeling of fatigue was assessed on a visual analog scale before exercise. Exercise tests were performed on a treadmill. The speed and the gradient were increased incrementally until the maximum capability was reached. We measured VO2, VCO2, measured VO2max on theorical VO2max (VO2m/VO2t), respiratory rate(RR) and minute ventilation (Ve) with a mass spectrometre, heart rate (HR) and arterial pressure (AP) with an automatic blood cuff and plasma venous lactates. Statistical analysis used ANOVA for repeated measures and Scheffe F-test for mean comparisons. P<0,05.

		PREOP	J3	J10
VO2 ml/min/m^2	R1	142±24	140±25	144±11
	Tmax	1024±231*	918±318*	942±207*
VO2m/VO2t%	max	0.88±0.09	0.78±0 13	0.86±0.13
VCO2 ml/min/m^2	TR1	134±24	116±13	136±16
	Tmax	1185±315*	989±351*	1021±302*
Ve L/min	TR1	9.5±2.0	9.2±2 0	9.6±2.3
	Tmax	58±20*	55±20*	54±19*
RR b/min	Tr1	13.75±4.5	16.0±4.0	14 0±4.7
	Tmax	31±7.5	33±9.9	32±8.0
Lactates mmole/l	TR1	1.38±0 48	1.35±.031	1.52±0.46
	Tmax	3.47±1.37*+	2.95±1.34*+	3 30±1.27*+
	TR2	2 6±.071*	2.2±.092*	2.8±10.03*
SAP mmHg	TR1	133±21	130±22	121±31
	Tmax	183±32*+	164±24*+	167±22*+
	TR2	126±29	126±14	130±21
HR b/min	TR1	67±8	71±11	69±11
	Tmax	148±24*+	129±25*+	139±23*+
	TR2	89±12*	97±25*	84±13*
VAS (0-10)	TR1	2.0±2.0	3.1±2.4	1.72±2.0

Results : mean age were 58.2±9,5 years. Sex ratio was 5males/3females. Results are displayed on table 1
TR1= at rest, Tmax=maximal effort,TR2=recovery(10min)
* P< 0,05 vs TR1, + P< 0,05 vs TR2

Conclusion: Muscular and cardio-respiratory capacities are not impaired by laparoscopic cholecystectomy. This results are in agreement with the lack of subjective fatigue and confirmed the excellent tolerance of this surgical procedure.

Références :

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A.36

PULMONARY FUNCTION AFTER LAPAROSCOPIC CHOLECYSTECTOMY

P. Rotbøll Nielsen, J Brushøj, C. Sonnenschein
Department of anaesthesiology, Central County Hospital, DK
4800, Nykøbing F. Denmark

Background and goal of study: After conventional cholecystectomy a 30% reduction in functional residual capacity (FRC) is observed on the first postoperative day. FRC returns to normal preoperative level after one to two weeks. The aim of this study was to measure the changes in pulmonary function after elective laparoscopic cholecystectomy. (LPC)

Material and methods: 12 ASA 1 patients medien ages: 44 (24-65 years) participated in the study. Obesity. preoperative abnormal lungfunction and peroperativ conversion to cenventional surgery were criteriss for exclusion. General anaesthesia: midazolam, fentanyl, N2O and atracurium. Assessment of pulmonary function was made with Medgraphic 1070 series S, the day before and 24 h. after operation. A Vitalograph was used for bedside measurement, 3 and 6 h. postoperatively. Pain therapy consisted of paracetamol 1 g x 4 amd morphine 5 mg on request. Postoperative pain was registered by VAS.

Results and discussion: Compared to preoperative levels the reduction at 24 h. for FRC was 8% and for total lungcapacity (TLC) 17%, both significant. Residual volume (RV) was unchanged. (Wilcoxon test for paired data) The postoperative reduction in forced expiratory volume in 1 sec (FEV-1) were: 30% 3 h, 33% 6 h and 22% 24 h. Forced vital capacity (FVC): 29 % 3 h, 28% 6 h and 25% 24 h. The changes in FRC were smaller than after open cholecystectomy. The study shows, that there is a parallel decline in FRC and TLC while RV was unchanged. The changes in FEV-1 and FVC are equivalent to other studies. The small decline in FRC should lead to less pulmonary shunting after LPC. LPC is now widely accepted and it is difficult to perform a controlled study between LPC and conventinal Gall bladder surgery, because randomization is impossible.

	FRC	TLC	RV
Preop.	3.13 L (2.30 - 4.66)	6,32 L (4.83 - 9.40)	2.39 L (1.33 - 3.39)
24 h. postop.	2.83 L (2.13 - 4.65)	5.28 L (2.94 - 8.08)	2.34 L (1.32 - 3.67)

Mean values and range

Conclusion: LPC is followed by a small but significant decline in FRC and TLC in otherwise healty individuals.

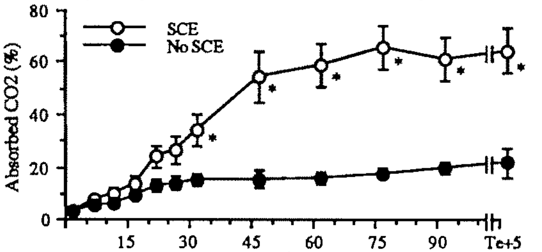
A.37

RESPIRATORY CHANGES INDUCED BY SUBCUTANEOUS EMPHYSEMA DURING LAPAROSCOPIC FUNDOPLICATION.

J.D. Chiche, J. Joris, M. Lamy.

Department of Anaesthesiology & Intensive Care Medicine
CHU LIEGE. B-4000 LIEGE, BELGIUM.

Background & goal of the study: CO_2 pneumoperitoneum (CO_2-PP) produces an increase in $PaCO_2$ partially explained by an increase in CO_2 production (VCO_2).[1,2] CO_2 subcutaneous emphysema (SCE) regularly occurs during laparoscopic fundoplication. Indeed, opening of the peritoneum overlying the diaphragmatic hiatus allows CO_2 to diffuse through the mediastinum to the cervico-cephalic region. In case of SCE, end-tidal PCO_2 ($PetCO_2$) further increases, sometimes requiring marked hyperventilation. We therefore investigated respiratory changes induced by CO_2 SCE.
Materials and Methods: Twenty five fully informed ASA I-II patients scheduled for laparoscopic fundoplication were included in the study. Total intravenous anaesthesia was induced and maintained with propofol, sufentanil and atracurium. Ventilation (FiO_2 0.4), initially set at 100 $ml.kg^{-1}.min^{-1}$, was adjusted to maintain $PetCO_2$ between 30-40 mmHg. The following parameters were measured: arterial blood gases, $PetCO_2$ (Datex Capnomac®), VCO_2 and O_2-uptake (VO_2) (Datex Deltatrac®), minute ventilation (MV) and peak airway pressure (Paw) (Siemens Servo 900C). Baseline measurements were registered, and parameters were recorded after the beginning of insufflation every 5 min during the first 30 min then every 15 min. Absorbed VCO_2 ($Abs.VCO_2$) was defined as measured VCO_2 - metabolic VCO_2 ($Mb.VCO_2$ = measured VO_2 x baseline respiratory quotient). Percentage of increase in absorbed CO_2 was calculated as $Abs.CO_2 = Abs.VCO_2 / Mb.VCO_2$. A score was used to quantify SCE: 1 point if cervical, cephalic, or thoracic SCE, 2 points if bilateral, and 3 if very marked SCE. Data (mean ± SEM) were analyzed by ANOVA and Mann and Whitney U test.



*: $p<0.005$ as compared to "NoSCE" group ; Te+5: 5 min post exsufflation

Results: During CO_2-PP without or prior to the development of SCE, a 16.9 % increase in VCO_2 was observed. Sixteen of 25 patients developed SCE 47 ± 6 min after the beginning of insufflation. SCE resulted in a significant increase in absorbed CO_2 (Fig 1). $Abs.CO_2$ was correlated to the severity of SCE ($r=0.77$, $P<0.001$). A significantly greater increase in MV was required to limit hypercapnia in the SCE group (33.3 ± 6 % vs 8.9 ± 5 %, $p<0.01$). Nevertheless, $PetCO_2$ and $PaCO_2$ significantly rose in the SCE group, thus leading to a significant decrease in pH (7.33 ± 0.01 vs 7.38 ± 0.01, $p<0.01$).
Conclusion: This study confirms absorption of CO_2 through the peritoneum during CO_2-PP. SCE results in a significant increase of absorbed CO_2 proportional to the severity of SCE, leading to hypercapnia. Hyperventilation, sometimes insufficient to avoid hypercapnia, is thus necessary and may complicate the anaesthetic management of laparoscopy. These data suggest that CO_2 absorption is limited as long as CO_2 remains in the abdominal cavity, probably due to collapse of peritoneal vessels secondary to increased intraabdominal pressure.

References

1.Can J Anaesth 1992,39:677; 2. Anesthesiology 1992, 77:A37.

A.38

PEEP FOR TREATMENT OF INTRAOPERATIVE PNEUMOTHORAX DURING LAPAROSCOPIC FUNDOPLICATION.

JD Chiche, J Joris, M. Lamy.

Department of Anaesthesiology & Intensive Care Medicine.
CHU LIEGE. B-4000 LIEGE, BELGIUM.

Background & goal of the study: Laparoscopic fundoplication, routinely performed in our institution for more than 2 years, was associated with 6 symptomatic intraoperative pneumothoraces (PNO) (5%). Tears of the parietal pleura probably occurred during dissection of the left crux of the diaphragm. This complication, well tolerated, usually required only moderate increase of O_2 concentration and minute ventilation. PNO disappeared before the end of surgery or within 1h after surgery without thoracocentesis. We therefore monitored patients scheduled for laparoscopic fundoplication to document the development of PNO, and to evaluate the benefit of PEEP to treat PNO.
Materials & Methods: Patients scheduled for laparoscopic fundoplication from January to June 1993 were extensively monitored. We measured end-tidal PCO_2 ($PetCO_2$), minute ventilation (MV), thoracopulmonary compliance (C), peak airway pressure (Paw) using a Datex Capnomac Ultima® SV, O_2 uptake and CO_2 production with a Datex Deltatrac®, and arterial blood gases. We report data (Table 1) of 6 patients who developed a PNO during CO_2 pneumoperitoneum (14 mm Hg).

	$PetCO_2$ mmHg	$PaCO_2$ mmHg	VCO_2 ml/min	PaO_2 mmHg	P_{aw} cmH_2O	MV l/min	C: ml/ cmH_2O
#1 T1	35	37	202	162	24	8.4	34
T2	37	39	268	118	31	9.8	28
T3	36	36	272	121	29	10.4	35
#2 T1	39	-	-	-	29	7.4	27
T2	45	-	-	-	38	8.5	20
T3	39	-	-	-	27	8.4	44
#3 T1	29	40	138	207	25	7.5	30
T2	44	59	303	143	39	7.8	20
T3	35	48	270	164	42	10.1	24
#4 T1	32	37	173	162	21	7.5	36
T2	40	48	318	133	31	9.4	30
T3	35	44	308	151	32	11.4	35
#5 T1	43	-	-	-	16	4.6	29
T2	58	-	-	-	26	4.7	15
T3	47	-	-	-	30	6.8	27
#6 T1	31	37	140	216	24	6.9	29
T2	41	48	209	165	28	6.9	24

T1 = during pneumoperitoneum but before PNO, T2 = PNO, T3 = 15 min after 5 cm H_2O PEEP; PEEP was not used in #6.

Results: Left PNO was diagnosed in every patient by hypoventilation of the left lung. Endobronchial intubation was excluded in all patients. Fluoroscopy was used in 2 patients and confirmed the diagnosis. PNO developing during CO_2 pneumoperitoneum induced an increase of VCO_2, $PaCO_2$, and $PetCO_2$, a decrease of PaO_2, and required an increase of MV. C decreased and subsequently Paw increased. In these cases, the use of PEEP appeared sufficient to inflate the collapsed lung without further increase in Paw and allowed us to avoid thoracocentesis. Neither intraoperative fluoroscopy neither chest X-ray performed immediately after surgery showed residual pneumothorax nor major atelectasis after PEEP treatment. Furthermore, this non-invasive treatment partially corrected the increased CO_2 absorption and the decreased PaO_2 both due to PNO, and reduced the requirement for hyperventilation.
Conclusion: In conclusion, anytime $PetCO_2$ abnormally increases with no apparent cause such as subcutaneous emphysema, the diagnosis of PNO must be evoked. If PNO is confirmed by lung auscultation, PEEP should be applied. Careful monitoring of $PetCO_2$, C and Paw are helpful in the early diagnosis of PNO.

A.39

VARIATIONS OF ARTERIAL PCO2 (PaCO2) DESPITE OF CONSTANT END TIDAL PCO2 (PETCO2) DURING CO2 PNEUMOPERITONEUM

SEGUIER J.C., HILBERT U., SINDA P.
Dept. of Anaesthesia.
Centre Hospitalier Général
78104 SAINT-GERMAIN-EN-LAYE - FRANCE

The aim of the study was to compare PaCO2 and pH sampled at fixed intervals to continously monitored PETCO2 during elective laparoscopic cholecystectomy. Sixty patients without respiratory fail were included, all ASA I or II. The anaesthesia protocole applied was the same for all patients. The initial tidal volume was 10ml/kg, the ventilation rate 10/mn adapted after 15 minutes' intervals if PETCO2 exceeded 5 KPA.

Hypercapnea and respiratory acidosis shown by blood gas analysis (BGA) contrast with a pratically inchanged PETCO2 so that we observed an increasing PaCO2-PETCO2 gradient. There was despite PETCO2 inferior to 5KPA an insufficient control of CO2 elimination by capnometer monitoring. Similar results have been already reported by Mäkinen M.T. and all (1).

		DURING CO2 INSUFF			AFTER	
	Control	**15 mn**	**60 mn**	**120 mn**	**30 mn**	
PaCO2 (KPA)	4.93 ±0.9	5.34 ±0.72	5.45 ± 0.7	5.53 ± 0.74	5.94 ± 0.68	*
PETCO2 (KPA)	4.18 ± 0.6	4.62 ** ± 0.6	4.5 ± 0.59	4.5 ± 0.55		
A-ET grad	0.71 ± 0.89	0.71 ± 0.54	0.96 ± 0.53	1.04 ± 0.66		
pH	7.41 ± 0.04	7.37 ± 0.04	7.36 ± 0.045	7.35 ± 0.045	7.33 ± 0.024	*

* $p<0.05$ between control and all subsequent values
** $p<0.05$ between control and fifteen minutes values

PETCO2 monitoring during CO2 pneumoperitoneum isn't trustworthy at least after 60 minutes of insufflation. It seems worth-while using BGA to control PaCO2-PETCO2 gradient and evaluate respiratory acidosis. This acidosis , although having had no clinical incidents in our study, suggests that there could be a security time limit for laparoscopy and that the probable body retention of CO2 illustrated by pH and PaCO2 30 minutes after CO2 exsufflation should lead to maintain ventilation during that time to ensure best CO2 elimination and thus quick correction of pH and capnea values.

(1) Arterial to end-tidal PCO2 difference during carbon dioxide pneumoperitoneum.
Mäkinen MR.,Aromaa U.
Acta Anaesthesiologica Scandinavica.
Supplementum 100, Vol 37, 1993.

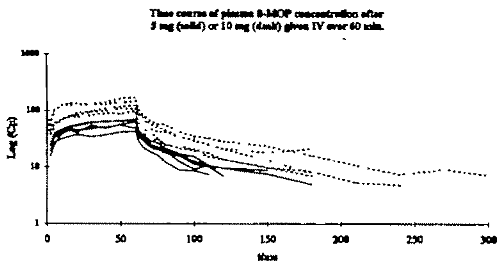
P, 25 328.

A.40

PHARMACOKINETICS OF 8-METHOXYPSORALEN (8-MOP) IN HUMANS PRIOR TO ROUTINE USE FOR PLATELETS DECONTAMINATION: PRELIMINARY RESULTS.

V. Billard, PL. Gambus, C. Minto, J. Barr, SL.Shafer
Department of Anesthesia, Stanford University, CA94305, USA.

Background &goal: Bacterial contamination of transfused blood cells or platelets is a severe complication that may occur both in the OR as in hematologic ICU. A new method of photochemical decontamination using 8-MOP and UVA has been recently proposed to inactivate pathogenic bacteria in platelet concentrates (PC). As residual 8-MOP (7.5 mg) will be transfused with each 300 ml of PC, the pharmacokinetics of this drug after intravenous administration has to be precised.
Methods: Adult healthy volunteers received IV 8-MOP in normal saline over 60 min. at 3 dose levels (5, 10 or 15 mg, n=6/dose). Vital signs and side effects were monitored, and repeated arterial blood samples were drawn for 8-MOP concentration assay during the infusion and for 9 hr after. Whole blood (WB) and plasma 8-MOP levels were measured using chromatographic eluates and dual wavelength HPLC (sensitivity limit: 15 µg/L for WB and 5 µg/L for plasma). PK analysis was performed using NONMEM program. Only 5 subjects in the 5 mg group and 5 in the 10 mg group are presented in this preliminary report.
Results: No adverse effects were observed during infusion or after.
At each dose, both plasma and WB 8-MOP levels (ng/ml) declined rapidly after cessation of 8-MOP infusion (fig. 1).



For all subjects the time course of plasma 8-MOP levels could be described by a 2 compartment PK model. The subjects weight was a relevant covariate in the estimation of the PK parameter. The total plasma clearance was 7.53 ml.kg^{-1}.min and the intercompartment clearance was 13.8 ml.kg^{-1}.min^{-1}. The volume of central compartment was 61.4 ml.kg^{-1}, and the volume of distribution at steady state was 535.4 ml.kg^{-1}.
Conclusion: After a single IV infusion, IV 8-MOP is rapidly cleared and does not have adverse effects. PK parameters are similar to those obtained after oral administration. These results allow to perform further pharmacodynamic studies on 8-MOP for bacterial inactivation before platelet transfusion.

A.41

BLOOD REQUIREMENTS IN VASCULAR SURGERY DURING 1 YEAR PERIOD

M.Gosgnach,S.Mouren,G.Godet,A.Balma,M.Ismail, A.Pironkov,M.Bertrand,P.Viars
Department of Anesthesiology,Hopital Pitié-Salpêtrière , Paris, France

Introduction: To avoid homologous transfusion is a major concern during vascular surgery.To propose the most appropriate strategy for autologous transfusion , we need to perfectly appreciate blood requirements during vascular surgery.The aim of our study was to evaluate blood products requirement for different types of vascular procedures .
Methods: From August 92 to July 93,all patients scheduled for vascular surgery were prospectively studied in this study. We evaluated the amounts of autologous (predonation:AB,intraoperative:IOB) and homologous (HB) blood products received by each patient in both the intraoperative and the postoperative periods Then these parameters were compared for to the most common vascular surgical procedures:abdominal (AAS),thoracoabdominal(TAS) aortic surgery, carotid surgery (CS), lower limbs revascularisation (LLR), isolated renal or visceral artery surgery (RVS) and surgery for septic prothesis (SP).
Results: The number of blood products perioperatively transfused in the 760 studied patients are reported in the table (n= units/patient)

	patient	AB(n)	HB(n)	IOB(n)	HB=0
AAS	213	1.6	2 6	1.3	72%
TAS	51	0.6	11.3	15 6	0%
CS	140	0.04	0 3	0	99%
LLR	107	0.06	0.7	0	77%
RVS	21	0.6	2.5	0.1	43%
SP	33	0	10.3	0	0%

Conclusion : These results confirm the low rate of transfusions in (CS) .A predonation programm is not indicated for this procedure.They also point out the real benefit of blood predonation in (AAS). By contrast the lack of accuracy for (TAS) can not be improved because of the dramatic blood loss in this surgery The percentage of patients scheduled for LLR or SP receiving HB can not be reduced because of the absolute contraindications of autologous transfusion (SP) or the difficult organization of predonation (LLR) faced in these 2 pathologies.The surprisingly high percentage of patients scheduled for (RVS) who required HB transfusion led us to routinely proposed them for predonation .

A.42

Influence of Blood Transfusion on Cardiac Index and End-tidal Carbon Dioxide Tension Relationship in Anesthetized Patients

Deriaz H, Vrillon M, Delva E, Lienhart A
Dpt Anesth., Saint Antoine Hosp., Paris FRANCE

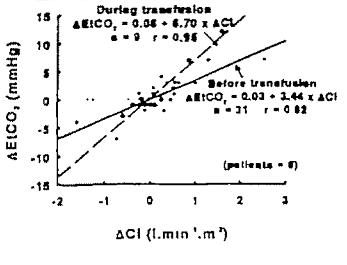
Introduction: Changes in end-tidal carbon dioxide tension ($\Delta EtCO_2$) has been shown to be correlated with changes in cardiac index (ΔCI) in anesthetized patients [1]. Blood transfusion may increase the transfer of CO_2 and therefore modify this relationship. The aim of this study was to further examine the influence of blood transfusion on the CI-EtCO2 relationship in anesthetized patients.

Material and methods: Concomitant changes in $EtCO_2$ and CI were studied in 6 patients (62±8 y. (m±sd)), needing invasive hemodynamic monitoring for hemorragic surgery. After induction, patients were intubated and mechanically ventilated with a Dräger^R AV1 anesthesia machine. $EtCO_2$ was monitored on a Datex^R Capnomac infrared analyzer calibrated before anesthesia and connected at the endotracheal tube. Ventilation was adjusted to reach an $EtCO_2$ of 34±2 mmHg within the first 20 min of anesthesia and this pattern of ventilation was maintained constant throughout the study. CI was measured in triplicate with a Baxter^R COSet through an Edwards^R Swan-Ganz catheter on a Hewlett Packard^R Merlin CO computer. $EtCO_2$ and CI were recorded every 30 min on two periods.before and after the beginning of transfusion The recorded CO_2 was the rounded mean $EtCO_2$ over the triplicate measurement of CI. The study was interrupted at the end of transfusion or when the ventilation was changed for clinical reasons. Changes were considered between two consecutive measurements of the same period. ΔCI were plotted against concomitant $\Delta EtCO_2$. Correlations were performed for each period: before and during transfusion.

Results: Patients received 2.7±1 0 PRBC in 35±7 min.pack^{-1}. 31 simultaneous measurements of ΔCI and $\Delta EtCO_2$ were recorded before blood transfusion, and 9 during transfusion. Results are presented in the figure. The slopes of the two correlations are significantly different ($p<.001$).

Discussion: The linear relationship between ΔCI and $\Delta EtCO_2$ is not abolished by blood transfusion, but the slope is significantly increased, suggesting a rise in the transfer of CO_2 : the blood transfusion increases the CO_2 transfer probably because of anaerobic metabolism during storage and because of the rapid metabolism of the transfused citrate by the liver. In the anesthetized mechanically ventilated patient, changes in CI are associated during blood transfusion with two-fold larger changes in $EtCO_2$ than before transfusion.

1. Deriaz et al, Anesthesiology 1993, 79 : A509.



A.43

HIGH DOSE INTRAVENOUS IRON SUPLLEMENTATION FACILITATES AUTOLOGOUS BLOOD DONATION

A.M. Schulte-Tamburen, M. Tryba, F. Rost, M. Zenz

Department of Anaesthesiology, Intensive Care Medecine and Pain Therapy,
University Hospital Bergmannsheil, Bochum, Germany

Background: Up to now autologous blood donation in most cases is coupled with oral iron substitution. Recently it has been shown that the effect of rh-erythropoietin could be enhanced by oral plus additional intravenous iron administration laying emphasis on iron therapy as a critical factor during autologous blood donation (1). We have conducted a randomized controlled study to determine the effectiveness of intravenous iron to increase the volume of preoperatively collected autologous blood.

Materials & methods: After approval of the local ethical committee twenty patients undergoing elective orthopaedic surgery with a predicted blood loss of at least 3 units were included. The patients were randomly assigned either to the intravenous iron group or to the control group. The donation period covered 3 weeks and included six visits within an interval of 3 to 4 days for evaluation and possible donation. At each visit, if the hematocrit was 34 percent or above, one unit of blood was collected: 400 ml of female and 450 ml of male patients. Thus, a maximum of 6 units could be collected. At each time the patient received an infusion of 500 ml NaCl 0,9% + 200 mg iron saccharate or 500 ml NaCl 0,9% over 30 minutes depending on the study group.

Results: The demographic parameters of the two groups were similar, as well as the baseline clinical and laboratory data. Patients treated with intravenous iron donated a significantly greater amount of autologous blood than did patients in the control group.

	Control	Iron
Age (y)	58.9 ± 12.8	67.4 ± 9.7
Weight (kg)	67.0 ± 11.9	68.8 ± 8.7
Height (cm)	163.7 ± 7.3	168.5 ± 6.5
Baseline Hb (g/100ml)	11.8 ± 7.3	12.0 ± 0.6
Donated Units (N)	2.71 ± 1.0	4.17 ± 1.5
Donated Blood (ml)	1136 ± 266	1833 ± 593*

* $p < 0.05$

In both groups the amount of donated blood correlated with the predicted blood volume. No adverse events were observed throughout the study.

Conclusions: Intravenous administration of iron does not depend on enteral resorption, which seems to be a limiting factor of oral iron supplementation. High dose intravenous iron was highly effective in facilitating autologous blood donation and was safe if infused over 30 minutes.

References: 1. F. Mercuriali et al., Transfusion 1993; 33:55

A.44

COMPARATIVE ANALYSIS OF COAGULATORY PROTEINS AFTER RETRANSFUSION OF POSTOPERATIVELY SALVAGED NON-WASHED AND WASHED AUTOLOGOUS BLOOD

Singbartl, G., Röhrs, E., Asmussen, C., Schleinzer, W.

Dept. Anaesthesiology, Intensive Care and Transfusion Medicine, ENDO-CLINIC, D-22767 Hamburg

Retransfusion of postoperatively salvaged blood is continuously gaining importance among the patient's blood supply. According to the autologous transfusion system (ATS) applied this can be done by either cell-separation and cell-washing (ATS III), and thereby eliminating debris, platelets, white blood cells as well as the greatest part of the autologous plasma, which results in autologous washed red blood cells, or by retransfusion of non-washed (ATS II) autologous 'whole blood', and thereby administering autologous red blood cells as well as debris, 'ghosts', free haemoglobin, activated/inactivated coagulatory proteins, platelets and white blood cells. Therefore, one of the most relevant questions by retransfusion of salvaged autologous blood is, to what extent is the patient's coagulatory system influenced by retransfusion of non-washed (ATS II) or washed (ATS III) salvaged autologous blood, respectively.

This prospective randomized study has been performed in 40 patients undergoing elective operation of the knee-joint. Postoperatively, non-washed blood was collected in the Solcotrans-Orthopaedic-System (600 ml) containing 20 ml of ACD, while blood to be washed prior to retransfusion was collected in a 600 ml collecting unit containing 10.000 IU of heparin. Each patient obtained one unit of salvaged blood, only. Blood samples of the patients were drawn immediately prior to retransfusion (T1), 5 minutes (T2), 15 minutes (T3), 24 hours (T4) and 4 days (T5) following retransfusion, and were analyzed for clotting proteins as given in below. Statistical analysis was performed (by C. R. Valery, Boston) by using a 2-way analysis of variance with repeated measurements of one factor; t-test was performed for comparing pre- to posttransfusion values (changes over time) as well as those of ATS-II- versus ATS-III-group. Results are given as mean-values ± SD; statistical significance has been set with $P \leq 0.05$.

FV (%): T1: 88 ± 5.4 vs 89 ± 12.3; T2: 88 ± 7.1 vs 91 ± 10.0; T3: 89 ± 6.4 vs 93 ± 10.9; T4: 93 ± 8.5 vs 95 ± 10.3; T5: 99 ± 9.5 a vs 101 ± 9.8 b.
Fibrinogen (mg/dl): T1: 422 ± 144 vs 427 ± 112; T2: 422 ± 147 vs 462 ± 120; T3: 424 ± 144 vs 455 ± 128; T4: 469 ± 165 vs 535 ± 144; T5: 433 ± 174 c vs 548 ± 131 c.
D-dimer (ng/ml): T1: 407 ± 284 vs 544 ± 261; T2: 730 ± 346 a vs 309 ± 976 b; T3: 778 ± 366 vs 726 ± 340 b; T4: 606 ± 441 vs 571 ± 371; T5: 407 ± 436 vs 442 ± 374.
F1/F2 (µM/l): T1: 4.2 ± 2.2 vs 4.1 ± 3.3; T2: 7.4 ± 4.0 a vs 6.2 ± 4.5 b; T3: 6.8 ± 3.9 vs 5.7 ± 3.7; T4: 4.3 ± 3.3 vs 4.3 ± 3.6; T5: 3.6 ± 2.7 vs 2.9 ± 2.5.
TAT (µg/l): T1: 60 ± 47 vs 64 ± 60; T2: 132 ± 61 a vs 106 ± 60 b; T3: 108 ± 54 vs 90 ± 43; T4: 64 ± 48 vs 49 ± 35; T5: 43 ± 33 vs 26 ± 19.
Prot C (%): T1: 78 ± 30 vs 82 ± 29; T2: 77 ± 28 vs 86 ± 29; T3: 79 ± 32 vs 85 ± 27; T4: 76 ± 33 vs 80 ± 21; T5: 83 ± 33 vs 86 ± 21.
a, b: significance ($p < 0.05$) over time vs T1
c: difference significant ($p < 0.05$) ATS II vs ATS III
While significant changes over time (a, b) can be demonstrated for the different coagulatory proteins both for ATS II and for ATS III, a significant difference between these two groups (c) is to be seen for fibrinogen, solely, on day four after retransfusion.

A.45

IS THERE A BENEFIT TO PROCESS BLOOD REMAINING IN CARDIOPULMONARY BYPASS (CPB) BY CELL SEPARATION TECHNIQUE ?

JF Baron, S Massonnet-Castel, L Gouyet, D Bensasson, A Fiemeyer, P Guibourt, O Ponzio, A Carpentier, MT Cousin

Departments of Anaesthesiology, Cardiac Surgery and
Transfusion Center - Hôpital Broussais -
96, rue Didot - 75674 Paris cédex 14 - France

Risks associated with transfusions have promoted various methods to minimize blood requirements during cardiac surgery. However, in patients with low haemorrhagic risk, the cost-benefit of blood conservation techniques is still a subject of controversy. In a randomized study, we compared the retransfusion of the blood remaining in the CPB circuit either processed with a cell separation technique (Cell-Saver IV, Haemonetics) or unprocessed using transfer ACD bags.
Methods : After informed consent was obtained and with Institutional Review Board approval, 100 consecutive patients scheduled either for valve repair or replacement, or coronary artery bypass grafting were included in the study. We excluded congenital heart diseases, aortic root surgery, endocarditis, redo operations at high haemorrhagic risk and patients with disorders of haemostasis. Inclusion in an autologous predonation program was performed as often as possible with the following contraindications : infection in progress, anaemia, positive serology for HIV or hepatitis, emergency or organitional problems. Intraoperative use of aprotinine was restricted to redo surgery and preoperative antiplatelet therapy. CPB was performed using a membrane oxygenator, a priming volume of 1500 ml and an arterial flow 2.0 l/min/m^2 under moderate hypothermia (28°C) Transfusion was indicated to maintain haematocrit (Hct) ≥ 25% during bypass and ≥ 30% during the post-operative period. In the "Cell Saver", group intra-operative blood loss and blood remaining in the CPB was processed and retransfused. In the "Unprocessed" group, blood remaining in CPB was directly transfered in ACD bags. Blood loss was assessed at the end of the ICU stay. Hct, amounts of autologous and homologous blood products, administered were recorded repeatedly until hospital discharge.
Results : The study was completed during a 6 weeks period. By a game of chance, 50 patients were included in the predeposit program, 27 in the "Cell-Saver" group and 23 in the other group. No significant difference in demographic data, surgical procedures, duration of CPB, volume of cardioplegia was observed between the 2 groups. Preoperative coagulation tests, use of heparin and protamine were not different between the 2 groups. At any time during the study, Hct was similar in both groups No significant difference in blood loss, homologous and autologous transfusion was observed. Finally, the number of patients receiving homologous transfusion was not different in both groups
Conclusion. In patients at low haemorrhagic risk, there is no benefit to process blood remaining in CPB circuit by a cell separation technique.

	Cell-Saver	**Unprocessed**
Blood loss (ml)	807 ± 60	710 ± 52
Autologous Packed Cells	1.16 ± 0.19	1.18 ± 0.18
Homologous Packed Cells	1.72 ± 0.037	1.96 ± 0.37
HomologousTransfusion (patients, %)	24 (48 %)	22 (44 %)

A.46

METABOLIC ACIDOSIS DEVELOPING DURING INTRAOPERATIVE (EXTREME) NORMOVOLAEMIC HAEMODILUTION

Singbartl, G., Doßmann, H., Frankenberg, Ch.,
Schleinzer, W.

(Dept. Anaesthesiology, Intensive Care and Transfusion
Medicine, ENDO-CLINIC, D-22767 Hamburg)

Normovolaemic haemodilution (NHD) is the easiest and least expensive method among the various autologous transfusion techniques. However, its efficiency is limited by the potential risk of an inappropriate oxygen supply of the tissue. By applying NHD routineously in elective surgery, development of a metabolic acidosis is to be demonstrated. The question arising is, what are the causality and the potential relevance of this metabolic acidosis.

This prospective study has been performed in 135 patients undergoing major operation of the hip or knee joint with an expected blood loss of ≥ 2000 ml. Anaesthesia has been administered by combining spinal and epidural anaesthesia with plain bupivacain 0.5 %. Acid-base-status, anion-gap, haemoglobin, electrolytes, PaO_2 and $PaCO_2$ have been determined both prior to starting anaesthesia/NHD and after 500/1000 ml of NHD as well as during the operative procedure with replacement of blood by polygeline, solely, and in any case prior to transfusion of autologous/homologous blood. Statistical analysis has been performed stepwise: 1st by the correlation between two variables (PEARSON and BRAVAIS), 2nd by the rank-correlation (SPEARMAN) of two variables in dependence on the extent of haemodilution and 3rd by the multiple correlation of variables focused on the change of pH. Statistical significance has been set with $P < 0.01$.

Applymg NHD as well as colloidal replacement of the intraoperative blood loss results in a statistically significant decrease of pH, haemoglobin, standard-bicarbonate, and base-excess, while no corresponding changes can be demonstrated for $PaCO_2$ or lactate. Rank-correlation dependent on the extent of NHD reveals high correlations of pH versus NHD ($R_{Sp} = -0.9643$; $P < 0.01$) as well as versus haemoglobin ($R_{Sp} = 1.0$; $P < 0.001$); the same accounts for the rank-correlation of base-excess versus NHD ($R_{Sp} = 0.9375$; $P < 0.01$) as well as versus haemoglobin ($R_{Sp} = 0.9375$; $P < 0.001$). Again, no significant correlations can be demonstrated for pH and base-excess, respectively, versus $PaCO_2$ and lactate. Multiple correlation analysis focused on pH results in a multiple correlation coefficient of $R = 0.9503$ and $R^2 = 0.9031$; demonstrating, that approximately 90 % of the variance of changes of pH can be considered to be correlated to the variance of dilutional induced decrease of the buffering capacity of the blood (dilutional acidosis). Most important, lactic acidosis is not the causality of the metabolic acidosis developing during intraoperative (extreme) normovolaemic haemodilution.

A.47

FIBRINOLYTIC ACTIVITY DURING INTENTIONAL NORMOVOLEMIC HEMODILUTION

D. Samson,* D. Arnaud, K. Bennourine, JC. Manelli.
Dept of Anaesthesiology, Dept of * Haemostasis
Hôpital Conception Marseille. France.

Background and goal of the study The effects of different plasma substitutes on hemostasis are well known ; the purpose of this study is to determine whether the use of Dextran 60000 PM modifies the fibrinolytic system during intentional normovolemic hemodilution (HDNI).

Materials and methods With institutionnel approval and informed consent 20 patients treated for hip arthroplasty under general anaesthesia were randomly assigned in 2 groups of 10 each. Group A had hemodilution using human albumen at 4 %. Group B had hemodilution using Dextran 60. The object was obtaining a hematocrit of 32 ± 2 %.Blood analysis were performed measuring fibrinogen, plasminogen, tissue plasminogen activator (TPA), plasminogen activator inhibitor (PAI) alpha-2-antiplasmine , and euglobuline lysis time (TLE). a) before hemodilution T1b) at the end of hemodilution T2 c) before restitution of the bags T3d) the day after T4.The results are defined by the average of the values and compared by a non parametric test (Krushall and Wallis).

Results and discussion The volume of blood taken is more or less 875 ± 17 ml. The replacement is then performed volume for volume with one or the other solution.The two groups can be compared regarding age, weight, volume of blood taken and replaced, initial (43 ± 3,7) and final (33 ± 1,7) hematocrit..There is no difference between the two groups concerning the volume of external bleeding during the procedure and the following 24 hrs. Studied parameters variations were similar in both groups. TLE decreases in a statistically signifiant manner at T2 and T4 in the group A compared to group B. There are no other signifiant variations between the two groups.

Conclusion According to the dosage of Dextran 60 used in the study, intentional normovolemic hemodilution does not lead to fibrinolysis. The modifications noted seem related to surgery..

Reference : (1) GOMEZ M.J.. Perioperative fibrinolytic kinetics. Curr. Surg. 44, 476-479, 1987.

	ALBUMINE			
	T1	T2	T3	T4
TLE	196 ± 50	180 ± 50*	135± 68	226± 30*
tPA	0,70±0,71	0,62±0,57	2,83±4,54	1,19±1,19
PAI	12,7±9,42	9 ±7,5	10,3 ± 7,5	40,3±25,4
	DEXTRAN			
	T1	T2	T3	T4
TLE	213±40	217,5±37	168±64	240
tPA	0,43±0,34	0,48±0,52	0,84±1,19	0,73±0,91
PAI	12,2±9,86	9,2±8,26	18,6±14,5	23,9±14,2

* $p < 0,05$

A.48

EFFECTS OF DIFFERENT INTRAVENOUS SOLUTIONS ON PLASMA OSMOLALITY

R. TALIB, S. JAMALI, K. BUTSCHER, P. RAVUSSIN, C. ECOFFEY

Département d'Anesthésie, Université Paris-sud, Hôpital de Bicêtre, Le Kremlin Bicêtre, France

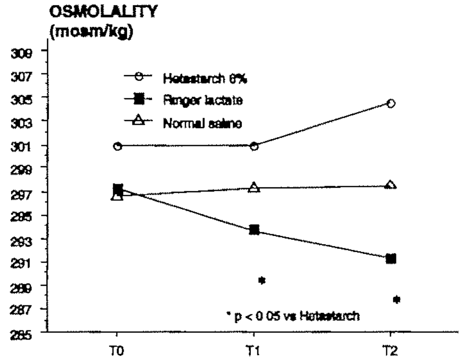
Background & goal of study: It has been shown that water in the normal brain is much more dictated by osmotic gradients than by hydrostatic or oncotic pressures (1). The goal of the present study was to compare the effect on plasma osmolality of the infusion of different currently used solutions.

Material & methods: 22 patients (ASA I-II) scheduled for lumbar intervertebral disc surgery were randomly allocated to three groups receiving 2000 ml of Ringer lactate solution (RL group, n = 7), 750 ml of hetastarch 6% (HS group, n = 8), or 2000 ml of normal saline (NS group, n = 7). Baseline plasma osmolality, Na, K, glycemia and urea were measured before induction of anesthesia (T0), after the infusion of 375 ml in the group 2, or 1000 ml in the groups 1 and 3 (T1), and at the end of infusion (T2). The laboratory measurements were accomplished without knowing the group of the patient. Data were evaluated for statistical analysis using two-ways and one-way ANOVA with the Bonferroni correction for multiple comparisons.

Results: The 3 groups were identical for age, weight and initial plasma osmolality (297 ± 5; 301 ± 6; 296 ± 8 mosm/kg). However, at T1 and T2, osmolality was significantly lower in the RL group compared to the HS (figure).

Conclusion: Both normal saline and 6% hetastarch maintain plasma osmolality, whereas Ringer lactate tends to decrease it. For that reason both solutions are well indicated in patients scheduled for intracranial surgery.

Reference: 1) MH Zornow et al. Anesthesiology 67: 936 - 41, 1987.



A.49

CHANGES IN PLASMA OSMOLALITY AFTER NACL 0.9% VERSUS RINGER-LACTATE AND HYDROXY-ETHYL-STARCH

Javier Dominguez, Patrick Ravussin, David Bracco, Claude Bachman *, Gery Boulard

Department of Anaesthesiology and *Central Clinical Chemistry Laboratory, CHUV, Lausanne, Switzerland

Introduction : During the last few years it has been shown that osmolality more than hydrostatic or oncotic pressures affects the water movements through the blood brain barrier (BBB) (1). Even a minimal decrease in osmolality of 3-5 mOsm/kg can create or aggravate significantly cerebral oedema. A gradient of only 1 mOsm/Kg between both sides of the BBB builds up a hydrostatic pressure gradient of about 20 mmHg (2). The aim of this study is to determine the effect on plasma osmolality of an infusion of 1) 2000 ml of NaCl 0,9% 2) 2000 ml of Ringer-lactate (RL) and 3) 750 ml of hydroxy-ethyl-starch (HES).

Material and Methods : After IRB appoval and informed consent, 60 ASA I-II patients, divided into 3 groups (NaCl, RL, and HES), age 20-60 years, weight ± 20% of the ideal body weight, undergoing elective intervertebral disc surgery, were studied. The following parameters were measured before induction (To) and after 2000 ml of cristalloids or 750 ml of HES (T1): plasma osmolality, ionogram, albumin, proteins and haemoglobin. The anaesthetic technique was identical in each patient: thiopental, fentanyl and vecuronium for induction, and isoflurane for maintenance.The results are expressed as means ± SEM. Statistical analysis used ANOVA and the Wilcoxon signed rank test. A value of $p < 0.05$ was considered as significant.

Results : The 3 groups were similar at To. In particular, osmolality was for NaCl 288.1±0.9 mOsm/kg, for RL 288.3±0.8 mOsm/kg, and for HES 287.3±0.8 mOsm/kg. By the end of the infusion mean osmolality increased significantly in all groups (NaCl, by 5.5±1.4 mOsm/kg, RL by 2.0±0.6 mOsm/kg, HES by 5.2±0.8 mOsm/kg) ($p < 0.01$) (Figure 1).The increase in osmolality was sifignificantly higher in the NaCl and HES groups than in the RL group ($p < 0.03$) (Figure 1).

Discussion : Osmolality, but rather its variations, is the determining factor which drives water from one side of the BBB to the other. 2000 ml of NaCl 0.9% increased significantly more osmolality than 2000 ml of RL. This increase although small helps maintaining cerebral water within the vascular bed and thus bears an anti-oedema effect. This result should be taken into account during fluid resuscitation in severe head injured patients.

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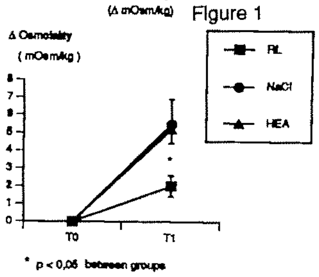

Figure 1

A.50

INFLUENCE OF INTRAOPERATIVE HIGH-DOSE HYDROXYETHYL STARCH 200 0,5 6% ON PLASMATIC ONCOTIC FUNCTION COMPARED TO ALBUMIN 5%

Vogt N, Roller D, Schönberger S, Georgieff M.
Clinic for Anesthesiology, University of 89075 ULM,
Steinhövelstr. 9, Germany

Therapy of blood loss with albumin 5% (HA) is expensive and occasionally unavailable. Medium-molecular-weight hydroxyethyl starch 200 0.5 6% (MW -HES) seems to affect coagulation lesser than high-molecular-weight HES. Even though albumin is commonly used as colloid component for extensive substitution of blood volume for keeping total serum protein threshhold levels above 50g/l in order to maintain oncotic function of plasma. We evaluated the ability of MW-HES to replace ALB solely as colloid component for the treatment of large blood losses.

Methods: In 2 randomized groups of 20 patients each undergoing large urological surgery (criteria of exclusion: anemia, coagulation disorders, renal dysfunction) we treated after institutional approval and informed consent up to 1000ml with colloid solution, from 1000ml up to 5000ml with packed red blood cells (PRBC) and colloid solution (1:1) and above 5000 ml with PRBC and fresh frozen plasma (1:1). Group HES received MW -HES and group HA albumin as exclusive colloid component. During the study period we compared total serum protein(TSP) colloid osmotic pressure (COP), and in the HES-group plasmatic HES concentration before operation after each 1000, 2000, and 3000ml of colloid application and at the end of the operation. Statistical testing: (Wilcoxon)

Results: Mean colloid volume(L): HES:2,5+ HA:2,1

ONCOTIC CHARACTERISTICS of Plasma MEAN (+/-SD)

Group	TSP[g/l]		COP [mmHg]		HES [g/l]		N	
HES	66.7	7.0	18.1	2.6			20	Pre-OP
HA	61.0	6.3	18.9	2.6			20	
HES	48.1	6.5*	18.0	2.4	4.1	1.4	20	1000ml
HA	59.3	5.6	18.9	1.6			20	
HES	33.7	6.3*	16.9	2.2+	7.4	1.9	14	2000ml
HA	64.4	7.0	18.6	2.1			13	
HES	27.8	4.4	16.7	2.9	8.0	1.9	8	3000ml
HA	61.7	0.0	18.6	0.0			1	
HES	37.9	14.4*	17.5	2.3	6.7	2.3	20	OP-End
HA	60.3	6.4	18.9	1.8			20	

+) $p < 0.05$ * $p < 0.01$

Conclusions: TSP level in the HES group decreased below a threshhold value of 50g/l, but COP values remained comparable with the HA group. With regard to the oncotic function of plasma MW-HES 200 0.5 6% is a safe colloid capable of replacing albumin 5% entirely as colloid component for treatment of even large blood losses intraoperatively.

A.51

INTUBATION - INDUCED STRESS RESPONSE: A COMPARISON BETWEEN DIRECT LARYNGOSCOPY AND BLIND ORAL INTUBATION

Pernerstorfer T, MD; Krafft P, MD; Chiari A, MD,
Krenn C, MD; Weinstabl C, MD
Dept. of Anaesthesia and Intensive Care Medicine,
University of Vienna, A - 1090 Vienna, Austria

INTRODUCTION: Intubation - induced cardio-vascular reactions are closely related to increased levels of catecholamines (1). The extent of stress response depends on premedication, induction agents as well as duration of intubation procedure (2). Recently, the Augustine Guide™ (AG-Augustine Medical, Eden Prairie, MN, USA), a new device enabling blind oral intubation has been introduced. In a previous study the clinical usefulness of the AG was demonstrated, although the intubation procedure lasted significantly longer compared to direct laryngoscopy (DL) (3). The aim of our study was to investigate, wether blind oral intubation causes a more pronounced stress-response than DL.

METHODS: After institutional approval, 20 normotensive patients (ASA I,II and Mallampati I,II) were included in our study. Patients were randomly assigned to either group DL (n=10) or AG (n=10). Induction was performed with 3mcg/kg fentanyl and 2mg/kg propofol. Muscle relaxation was achieved with 0.1mg/kg vecuronium bromide. Intubation was performed after disappearance of the fourth pike of TOF. Haemodynamic response as well as serum levels of dopamine, norepinephrine and epinephrine were determined prior to induction (timepoint I), immediately before intubation (II) and 5 minutes after intubation (III). Data are presented as mean ± SD and a p-value of < 0.05 was regarded significant.

RESULTS: Duration of intubation was 21±18 in group DL vs 50±7 in group AG (p<0.05) No significant differences in haemodynamic variables were observed between the groups. Dopamine was not detectable in any serum sample. Serum levels of epinephrine decreased slightly after induction and remained unaltered after intubation in both groups (table). Post-intubation norepinephrine values in group AG were significantly lower than preinduction values, while in group DL norepinephrine levels nearly returned to baseline (table).

time	I		II		III	
	DL	AG	DL	AG	DL	AG
HR	77±13	80±15	77±15	75±9	78±16	77±17
MAP	92±18	92±16	82±22	86±15	86±16	99±22
Dopa	0	0	0	0	0	0
Epi	59±22	53±108	45±8	47±54	43±14	45±66
Nor	206±77	267±136	119±41	121±44	173±66	109±30

HR=heart rate, MAP=mean arterial pressure, Dopa=dopamine, Epi=epinephrine, Nor=norepinephrine

CONCLUSIONS: Although blind oral intubation lasted significantly longer than direct laryngoscopy, haemodynamic stress response was equal and hormonal stress response was even less pronounced. Intubation using AG should not comprise patients suffering from cardiovascular diseases.

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A.52

DOSE-RESPONSE EFFECTS ON STRESS REACTIONS OF INTRAVENOUS CLONIDINE IN CABG-PATIENTS

P.J.Kulka, M.Tryba, B.Lakmann, F.Leurs, U.Ringeler

Department of Anaesthesiology, Intensive Care Medicine and Pain Therapy
University Hospital "Bergmannsheil", Bochum; FRG

Introduction: Dosage recommendation for clonidine vary considerably (1, 2). This study was performed to determine the appropriate dose of clonidine to suppress the reaction to laryngoscopy in CABG-patients.

Methods: After approval by the local ethical committee 48 patients were randomly and in a double blind fashion assigned to receive 2, 4 or 6 (Clo2, 4, 6) µg clonidine /kg or placebo (Clo0) as short term infusion over 15 min 30 min prior to induction of anaesthesia. Catecholamine plasma levels were determined at baseline t(t0), 30 minutes after start of the infusion (t1) and 1 min after beginning laryngoscopy (t2). Haemodynamic parameters were measured in predefined intervals. Additional medication to suppress haemodynamic reactions to intubation was given in a standardized manner. For statistical evaluation t-test was performed.

Results: Tachycardia due to laryngoscopy was attenuated in all Clo groups. Clo did not enhance the maximum blood pressure fall after induction of anaesthesia. Pressure response to intubation was significantly attenuated only in Clo4 and Clo6. Norepinephrine plasma levels in Clo4 and Clo6 were significantly lower at t1 and t2 (table).

	t0	t1	t2
Clo0	251 ±168	287 ±142	292 ±155
Clo2	364 ±94	242 ±70	322 ±72
Clo4	327 ±117	155 ±74 **a**	159 ±47 **a, b**
Clo6	279 ±112	116 ±65 **a, b**	166 ±79 **a, b**

Table: Norepinephrine plasma levels (mean ±sd); **a**= P<0.05 vs Clo0; **b**= P<0.05 vs. Clo2

In Clo0 and Clo2 signicantly more patients (6 and 5) required pharmacological interventions than in Clo4 and Clo6 (1 and 0).

Conclusion: 1. 2 µg Clo /kg did not significantly suppress the adrenergic response to intubation. **2.** ≥ 4 µg Clo /kg b.w. significantly attenuate the haemodynamic reaction to laryngoscopy and intubation. 6 µg Clo /kg were not more effective than 4 µg.

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2. Quintin L, et al: Effect of clonidine on the circulation and vasoactive hormones after aortic surgery. Br J Anaesth 1991; 66: 108-115

A.53

ATTENUATION OF HAEMODYNAMIC RESPONSES TO TRACHEAL INTUBATION WITH CLONIDINE AND NIFEDIPINE

Judit Méray*, Gyöngyi Horváth+, Melitta Roszik*,
Margit Szikszay+, György Benedek+

* Department of Anesthesiology and Intensive Therapy;
+Department of Physiology Albert Szent-Györgyi
Medical University, Szeged, Hungary

Background and goal of study: Alpha$_2$-adrenoceptor agonists and calcium channel blockers are widely used in the anaesthetic practice since they attenuate cardiovascular changes during intubation and decrease the need to supplement anaesthetic drugs. Animal experiments have recently revealed, that the calcium channel blockers potentiate the analgesic or anaesthetic effect of opioids and alpha$_2$-adrenoceptor agonists (1,2). The goal of our study was to determine the effects of clonidine (Catapresan) and nifedipine (Adalat) in low doses on the haemodynamic parameters during intubation and on the demands for opioid fentanyl and the muscle relaxant pipecuronium bromide (Arduan) in human anaesthesia.

Materials and methods: After institutional approval and informed consent, a double-blind study was made of 36 ASA II-III. patients aged 28-67 years scheduled for maxillo-facial surgery. The patients received beside a standardized praemedication and anaesthesia in Group I.: no further medication; in Group II.: clonidine in praemedication (2 μg/kg i.m.); in Group III.: nifedipine infusion (0.25 μg/kg/min) during surgery; in Group IV.: clonidine in praemedication and nifedipine infusion. Haemodynamic parameters (systolic and diastolic blood pressure -SBP, DBP-, heart rate -HR-) and ECG were monitored. ANOVA and t-test were used for statistics.

Results and discussion: In group I. SBP, DBP and HR rose significantly after laryngoscopy. Clonidine praemedication attenuated the tachycardic effect, while nifedipine infusion diminished the SBP increase. Coadministration of the two drugs attenuated SBP, DBP and HR changes as well. Nor clonidine neither nifedipine alone influenced the demand for fentanyl, although the two drugs together decreased it ($p<0.05$). The administration of clonidine (Gr. II. and IV.) significantly decreased the demand for pipecuronium.

Conclusion: Clonidine and nifedipine in low doses have favourable effects on the haemodynamic parameters during intubation, and decrease the need for opioid and muscle relaxant.

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A.54

ABSENCE OF PRESSOR RESPONSE FOLLOWING EARLY INSERTION OF LARYNGEAL MASK AIRWAY AFTER INDUCTION WITH FENTANYL & PROPOFOL

Green D, Ward B., Hughes N.

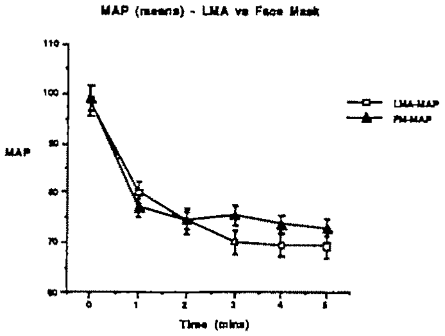
St. James' Hospital,
Dublin, Ireland

Background. Studies confirm that insertion of the laryngeal mask airway (LMA) is associated with a rise in heart rate (HR) and mean arterial pressure (MAP)[1], although this 'pressor response' is less than that associated with insertion of an endotracheal tube.[2] Personal observation suggested that the pressor response is masked if the LMA is inserted smoothly within 30 secs. after induction of anaesthesia. The goal of this study was to verify this hypothesis under controlled conditions.

Materials & Methods. 40 unpremedicated patients (ASA I & II) aged between 22-71 (mean = 41yrs) scheduled for minor elective surgery were randomly allocated into two groups (n=20). Both groups underwent a standard induction technique consisting of 50μg fentanyl iv., pre-oxygenation for 3 mins., followed by propofol at 40mg per 10 secs. until loss of consciousness (LOC) occurred. Group 1 had an LMA inserted smoothly (one attempt only) within 30 secs. after LOC. Group 2 had a face mask applied instead. Both groups underwent normocapnoeic hand ventilation ($E'CO_2$ 3.5-4.5kPa) with N_2O/O_2 (50:50) and 1% isoflurane for 5 mins. Monitoring of HR, MAP, $E'CO_2$ and SaO_2 were carried out by a blinded observer and data collected at 1 min. intervals. Results were analysed using paired t-Test. A p-value of <0.05 was considered significant

Results. The mean dose of propofol was 2.75 ± 0.58 mg/kg for the LMA group and 2.83 ± 0.47 mg/kg for the face mask group. Both groups displayed a drop in HR and MAP (see Fig.) from baseline values which was sustained. The fall in HR although consistent was not significant statistically. The fall in MAP was highly significant ($p<0.01$).

Conclusion. Early and smooth insertion of LMA after induction with fentanyl and propofol is not associated with a pressor response. This may be an important consideration in patients with compromised myocardial perfusion.



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A.55

INFLUENCE OF THE ANAESTHETIC TECHNIQUE ON THE INCIDENCE OF VENTRICULAR ARRHYTHMIAS IN PATIENTS UNDERGOING OPHTALMIC SURGERY.

N. Volpe, D. Guzzon, A. Benini, A. Gesini, G. Vitale, A.Vincenti*

Department of Anaesthesia and Cardiology*, University of Milan, Ospedale S. Gerardo, Monza, Milan, Italy.

Introduction

The presence of ventricular arrhythmias (VA) has been recognized as an indipendent predictor of morbidity and mortality in the perioperative period (1). Anaesthesia and surgery can influence the incidence and severity of VA in the perioperative period. The aim of the study was to assess the effect of 3 different anaesthetic techniques on the incidence and severity of VA in patients undergoing ophtalmic surgery showing VA on the preoperative ECG

Methods

100 patients, ASA I-III with VA on baseline ECG have been enrolled in the study and randomized to 3 groups, according to the anaesthetic technique. Group A induction with thiopentone and maintainance with Isoflurane and N_2O in oxygen; Group B induction with propofol and maintainance as in group A; Group C induction with propofol and maintainance with propofol+ N_2O (50%) in O_2. Holter ECG recordings were performed for 24 hours in the preoperative period and for the same amount of time in the postoperative period.

Results

The incidence and complexity of arrhythmias, in respect to baseline recording were not different among the groups. It has been noted, in Group C a trend short of statistical significance towards lack of anaesthesia induced changes in the incidence and patterns of VA in the perioperative period.

Conclusions.

Anaesthetic technique can influence the incidence and the patterns of VA in patients with ectopic activity on the baseline ECG Patients anaesthetised with propofol and N_2O present the lowest variability of the arrhythmic patterns.

1. Forrest JB, et al. Multicenter Study of General Anaesthesia. Predictors of severe perioperative adverse outcome. Anesthesiology 76: 3-15, 1992

A.56

INFLUENCE OF THE ANAESTHETIC TECHNIQUE ON THE INCIDENCE OF VENTRICULAR ARRHYTHMIAS IN NORMOTENSIVE AND HYPERTENSIVE PATIENTS UNDERGOING OPHTALMIC SURGERY.

N. Volpe, A Benini, D. Guzzon, A. Gesini, G Vitale.

Department of Anaesthesia, University of Milan, Ospedale S. Gerardo, Monza, Milano, Italy.

Introduction

Ventricular arrhytmias, expecially in patients with hypertension and coronary artery disease represent an unfavourable prognostic index in respect to the outcome following surgical intervention (1). It has been shown, in hypertensive patients, that pre-existing ventricular arrhythmias are always correlated to a worsening of the patterns of VA observed in the perioperative period Anaesthetic agents can induce modifications in the occurrence and severity of arrhythmias, furthermore, they can induce the occurrence of myocardial ischemia The aim of this study was to verify the cardiovascular safety of 3 anaesthetic techniques in normotensive or hypertensive patients

Methods

90 patients, ASA I-III, undergoing ophtalmic surgery, have been enrolled in this prospective study and randomized to 3 different anaesthetic techniques They were included according to the values of blood pressure and the presence on the baseline ECG of ventricular arrhythmias. The patients in group A received Thiopentone as an induction agent and anaesthesia was maintained with N2O+Isoflurane in oxygen. The patients in group 2 were induced with propofol and anaesthesia was maintained as in group 1. The third group of patients was induced with propofol and maintained with propofol and N2O in oxygen. Holter recordings were obtained for a mean of 19 hours preoperatively and 23 hours postoperatively

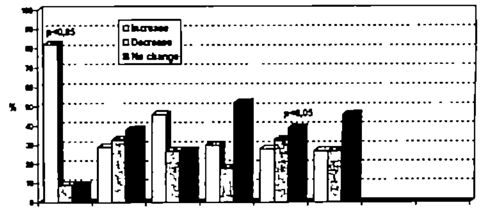
Results.

The variability in the incidence of arrhytmias in respect to baseline was not statistically significant among the 3 groups of normotensives In the hypertensives has been observed a statistically significant increase in the incidence of VA only in group A ($p<0,05$). Hypertensive patients in group C have shown the lowest variability in the incidence of arrhythmic pattern changes. This difference was statistically different ($p<0,05$) compared to group A

Conclusions

Hypertensive patients show a greater variability in arrhythmic patterns compared to normotensive subjects Propofol anaesthesia induces the lowest variability in the incidence and severity of ventricular arrhythmias in hypertensive patients undergoing ophtalmic surgery.

1. Forrest JB, et al Multicenter Study of General Anaesthesia. Predictors of severe perioperative adverse outcome Anesthesiology 76: 3-15, 1992



A.57

CONTINUOUS MEASUREMENT OF CORONARY SINUS OXYGEN SATURATION DURING VENTRICULAR TACHYCARDIA.

Y. Gallais, G. Lascault, J. Tonet, C. Himbert, Ph. Aouate,
F. Hidden, R. Frank, Guy Fontaine.

Hôpital Jean Rostand, Ivry, France.

The aim of this study was to assess the effects of VT on myocardial oxygen delivery and consumption balance (MDO2/MVO2) estimated by the coronary sinus oxygen saturation (ScsO2) variations.

In 45 patients (mean age 47 ± 27 years) with ischemic (20) and idiopathic (25) cardiomyopathy (EF: 0.31±0.11%) suffering from severe arrhythmias, sustained VT was induced for ablation procedure. Mean arterial pressure (MAP), filling pressure (PCWP, SvO2-Edwards oxymetry catheter - SAT 2), cardiac output (RVEF - Ref 1 Baxter) and ScsO2 (Edwards oxymetry catheter-SAT 1) were monitored. Myocardial lactate extraction (Ext - lactate oxydase PAP) and hemodynamic measurements were compared before and during VT (mean duration 18.4 ± 12.1 min).

	CONTROL (TO)	TV (T1)	p <0.01
HR (bpm)	63.7 ± 5.8	162 ± 16	
MAP (mmHG)	90.9 ± 14	50.4 ± 14.2	
CI (l/mm/m^2)	2.72 ± 0.14	1.52 ± 0.48	
RVEF (%)	0.30 ± 0.05	< 0 08	n = 20
PCWP (mmHg)	10.7 ± 2.3	22 1 ± 4.5	
SVRI (dyne.s.cm-5)	2125 ± 305	3076 ± 275	
SvO2 (%)	61.4 ± 11.2	42.3 ± 7.1	n = 20
ScsO2 (%)	39.3 ± 9 4	24.1 ± 8.2	
Lactate a (mmol/l)	0.61 ± 0.15	1.18 ± 0 36	
cs (mmol/l)	0.36 ± 0.12	0.98 ± 0.27	
ext (%)	41 ± 21	22 ± 17	

The ScsO2 drop is correlated with the SVRI increase (r=0.87, p<0 01), CI decrease (r=0.90, p<0.01) and with the myocardial lactate extraction decrease (r=0.71, p<0.05).

VT is responsible of a marked hemodynamic impairement related to loss of atrial transfert, shortness of filling period and abnormal sequence of ventricular activation. VT leads to a 40% ScsO2 drop, explained by a disturbance of MDO2/MVO2 : O2 supply reduction and O2 consumption enlargement. The ScsO2 level is important. At control, it is correlated with basic cardiac function ; all myocardial impairement leads to a less coronary reserve. During VT, 20% ScsO2 level is the threshold under which severe myocardial impairement occurs with deleterious complication probably due to a myocardial ischemia. ScsO2 level after the end of VT is linked to the ability of coronary blood flow to correct the O2 supply - demand disorders related to VT. All inadequate recovery results from myocardial ischemia with stunned myocardium reversible with catecholamines.

These results suggest that ScsO2, reflecting MDO2/MVO2 variations, can identify and quantify the myocardial impairement during VT, and might be considered as a safe index of cardiac hemodynamic tolerance, especially in patients with severe cardiomyopathy.

A.58

PROPOFOL INFUSION FOR MAINTENANCE OF ANEASTHESIA : CARDIOVASCULAR REPERCUSSIONS AND COSTS.

Luis Laranjeira, J Santos Pereira, Helena G Santos, Ilda Viana and Ana Paula Lopes Department of Anaesthesia - Hospital de Santa Maria, Lisbon, Portugal.

The economic costs involved in using propofol for the maintenance of anaethsia has been a factor limiting its use. The aim of the present study was to compare the cardiovascular stability and costs of this new intravenous agent with isoflurane, which is usually used in our hospital. 60 patients undergoing elective abdominal general surgery were randomised into two groups. One group received propofol for induction, and maintenance (2.5 mg $kg^{-1}h^{-1}$). (Group P). The other group received thiopental for induction and isoflurane for maintenance (Group I). Both groups were given fentanyl and midazolam before induction and nitrous oxide and oxygen during maintenance. Cardiovascular instability was determined by measuring changes in excess of 20% of basal systolic blood pressure and heart rate. Cost of anaesthetic usage during maintenance was determined in $\$kg^{-1}min^{-1}$. A greater stability was observed in group "P", for induction (systolic blood pressure, p<0.0), for intubation (s.b.p.,p<0.05 and diastolic blood pressure, p<0.01) and for maintenance (p<0.001) whilst significantly higher costs in group"I" (p,0.001) were noted.

It is concluded that propofol, besides providing a better cardiovascular stability, was also cheapter than isoflurane. Thus, its cost should not be considered as a factor limiting its use.

A.59

EFFECTS OF INTRAVENOUS URAPIDIL ON ISOFLURANE-INDUCED HYPOTENSION DURING EAR SURGERY

V. Deramoudt[1], N. Douet[1], Ph Rault[1], G. Nguyen[2], Y.Malledant[1]
[1] University Hospital Pontchaillou, Rennes, [2] Byk France, Le Mée sur Seine ; France

A bloodless surgical field during ear surgery requires a controlled hypotension with a stable and deep anesthesia. The adjunction of antihypertensive drugs to isoflurane anesthesia would be of some interests. We performed this randomized, controlled study in 31 ASA 1 patients between 18 and 65 (mean age of 38,5 years old) undergoing an ear surgery. Anesthesia was induced with thiopental (7mg/kg), alfentanyl (60μg/kg) and atracurium (0,5mg/kg), and was maintained with continuous perfusion of alfentanyl (1μg/kg/min) and with isoflurane (mean end expiratory concentration of 0,8 vol %). Ventilation was controlled with a 50/50 mixture of oxygen and nitrous oxide ($Fetco_2$=30 mmHg). Controlled hypotension started when the mean blood pressure (MBP) was $\geq$70mmHg. The patients were then randomly assigned to two groups : group urapidil + isoflurane (U) and group isoflurane alone (I). In group U, they received intravenously an injection of urapidil (0,4mg/kg) followed by a second one at the same dosage and a third one (0,8mg/kg) if needed, to obtain a MBP $\leq$60mmHg. Urapidil was then maintained (2,5mg/kg/hour). In group I, isoflurane was increased to obtain a MBP $\leq$60mmHg. Cardiovascular monitoring including heart rate, blood pressure was automatically recorded every 10 minutes, during anesthesia and the recovery. Surgical bleeding was assessed by the surgeon according to a numerical scale with 3 values (0=bloodless, 1=minor bleeding, 2=troublesome bleeding). A critical reaction time test was performed on the previous day and at 5 hours of the recovery period. The comparative assessment of the surgical field quality by the surgeon was significatively (Chi square test, $p \leq 0,05$) in favour of the group U:50% of bloodless fields, 41,7% of minor bleedings and 8,3% of troublesome bleedings were observed in group U as opposed to respectively 6,7%, 53,3% and 40% in group I. Time to obtain hypotension (I:30,3min$\pm$24; U:10,7min$\pm$9,8) and the consumption of isoflurane (I: 36,2ml ± 20,2; U: 21,65ml ± 8,7) were significatively higher (Mann and Whitney test, $p \leq 0,05$) in the group without urapidil. The means of MBP in the groups during the induced hypotension were similar (I: 61, 64mmHg ± 7,3; U:58,89mmHg ± 3,5) and their relative variabilities defined by the ratio of their standard deviation / MBP were not statistically different. An ANOVA with repeated measures applied to the analysis of heart rate throughout the surgical operation showed a significant increase ($p \leq 0,01$) in the group with isoflurane alone. The quality of the recovery of anesthesia was identical in both groups. Plasma renin activity was increased similarly.

In conclusion, this study therefore showed that intravenous urapidil, a 5HTA1 serotoninergic alpha 1 blocker, with an excellent safety profile and an easy use schaema was helpful in isoflurane anesthesia induced hypotension by reducing bleeding during ear surgery. We also pointed out other advantages like the reduction of the time to obtain hypotension by 66% and the consumption of isoflurane by 40%.

A.60

SPECTRAL ANALYSIS OF THE EFFECTS OF KETANSERIN ON BEAT-TO-BEAT CARDIOVASCULAR PARAMETERS IN HUMANS.

René Kingma, Gert-Jan Scheffer, Ben TenVoorde,
Karel Wesseling, Jaap de Lange.

Department of Anesthesiology, Institute for Cardiovascular
Research Free University (ICaRVU). P.O. Box 7057,
1007 MB Amsterdam, The Netherlands.

Background and goal of study: Ketanserin is an antihypertensive drug with affinity to both 5-hydroxytryptamine- ($5\text{-}HT_2$) and α_1-adrenoceptors. Ketanserin in blood pressure lowering doses causes no or only a transient reflex increase in heart rate (HR). Since the specific effects of ketanserin on the baroreflex mechanism are not fully understood we studied the effects of ketanserin on the regulation of blood pressure by analysis of beat-to-beat variability in cardiovascular signals.

Materials and methods: With informed consent and approval by the ethical committee of the Free University hospital Amsterdam, 2 x 5 mg of ketanserin was administered i.v. in 7 healthy volunteer subjects with an time interval of 5 minutes. First we measured spontaneous variability, then we asked the volunteers to breath at a fixed frequency of 0.1 and 0.25 Hz, (before and 30 minutes after the administration of ketanserin). The tests were performed in supine and in standing position. We also performed the Valsalva and the lying-to-standing manoeuvre. Blood pressure was measured non-invasively with the Finapres™. Analysis of the power spectrum of heart rate (HR) and systolic blood pressure (BP) variability can supply information about the "balance" of sympathetic and parasympathetic reflexes[1]. A low-frequency component (LO-FR, mainly sympathetic) was analyzed from a band of 0.06 Hz to 0.14 Hz. A high-frequency component (HI-FR, parasympathetic) was identified by the spontaneous variability frequency spectrum. Baroreceptor sensitivity (BRS) was determined by the ratio of spectral power of HR and BP.

Results and discussion: In agreement with previous data ketanserin did not affect HR. 30 minutes after the administration of Ketanserin there was no significant difference in spectral power, BRS, Valsalva-ratio or HR_{max}, however, in standing position a few volunteers tend to collapse at the Valsalva manoeuvre.

Conclusions: Ketanserin does not affect the baroreflex mechanism and has no effects on the autonomic nerve system. The collapse tendency in standing position can be explained by the need of vasoconstriction at the Valsalva manoeuvre, so Ketanserin is not an vasodilatator but inhibits vasoconstriction.

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A.61

POWER SPECTRAL ANALYSIS OF HEART RATE AND ARTERIAL BLOOD PRESSURE VARIABILITY DURING INTRAOPERATIVE UNINTENTIONAL HYPOTHERMIA

A. Pironkov, M. Portilla, M. Ismail, E. Buy,
P. Coriat, P. Viars
Département d'Anesthésie-Réanimation, G.H. Pitié-Salpêtrière, 75013 Paris, FRANCE

Unintentional hypothermia (UH) is common during the intraoperative period, and is know to have potential unfavourable cardiovascular effects. Power spectral analysis PSA of heart rate (HR) and arterial blood pressure, (BP) variability supplies valuable information about the autonomic nervous system (1). This study applied this method to assess change in autonomic nervous system associated with intraoperative UH.

Methods : 8 patients undergoing lower extremity vascular reconstruction under general anaesthesia were studied. Patient under betablocker therapy were excluded. In all patients, anaesthesia was induced with midazolam and fentanyl and maintained with additional fentanyl and isoflurane. A set of measurements was performed each time oesophageal temperature decreased by 1°C. We used a special algorithm and data acquisition system for PSA. HR variability : a high frequency component (RFa, parasympathetic) was identified by the respiratory frequency spectrum. BP variability : a low frequency component (LFa mainly sympathetic) was analysed. Measurements are "normalised" to represent the proportion of total variability in a specific frequency range, independent of changes in total variability power.

Results : A stable blood pressure was maintained throughout the surgical procedure. As shown in the table significant changes in PSA of HR appeared when central body temperature reached 34°C. These changes are not significantly correlated with the duration of anaesthesia, and not associated with HR change.

Intraoperative temperature	**HR Variability**		**BP variability**
	n	**RFa (%)**	**LFa (%)**
Post induction	8	14 ± 8	9 ± 5
35°C	7	16 ± 7	6 ± 4
34°C	6	25 ± 9*	7 ± 4

x ± SD, $p < 0,05$ ANOVA

Discussion : Our data indicate that intraoperative UH did not modify sympathetic activity but increased cardiac vagal tone. This shift of dominance towards the parasympathetic division of the autonomic nervous system, which is present although HR remained unchanged, must be taken into account when considering the potential cardiocirculatory deleterious effect of UH.

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A.62

HEART RATE VARIABILITY CHANGES INDUCED BY CERVICOTHORACIC EXTRADURAL ANALGESIA.

S Reiz, U Niklasson, E Nyström, U Wiklund.

From the Departments of Anaesthesia and Clinical Physiology, University of Umeå and the Department of Clinical Physiology, Västerås Central Hospital, Sweden.

***Background & goal of study*:** The influence of high extradural analgesia (EDA) on cardiac autonomic balance is subject to controversy (1). The present study uses spectral analysis of continuously recorded heart rate variability (HRV) in an attempt to further clarify this controversy.

Patients & methods: Seven patients with chronic osteoarthritic cervical pain were administered 15 mg of bupivacaine (3 ml) mixed with 40 mg (1 ml) of depomedrone via an extradural catheter with its tip at C6. HRV was recorded during 10 min in the supine position followed by two min of active standing before the EDA. After activation of the EDA, HRV was recorded over 30 min with the patients in the supine position followed by a 2 min recording in the active standing position. Data are presented as the means±SD of (a) total variability (e.g. the variance), and (b) of the contributions of the low (LF), medium (MF) and high frequency (HF) variabilities to total variability expressed in logarithmic units of Hz^2 as previously described (2). The MF values 20 min after EDA were also compared with MF values from 42 healthy individuals investigated while supine and standing without EDA. Analysis of variance and Student's t-test were used for the statistical analyses.

Results: The spread of the EDA was from C3±1 to T5±1. LF and MF variabilities decreased significantly in the supine position and changes were maximal 20 min after EDA. LF and MF variabilities returned to pre-EDA values when patients were standing up during EDA. The supine MF values 20 min after EDA were significantly lower than the corresponding values observed in the 42 patients without EDA.

Discussion: The decrease of MF and LF variabilities suggests a pronounced sympathetic blockade which was maximal 20 min after EDA. The lack of effect by EDA on LF and MF in the standing position was unexpected since standing normally activates the sympathetic system. Since EDA produces preganglionic blockade, this finding could be explained (a) by increased parasympathetic activity in the standing position, (b) by activity from segments caudal to those being blocked passing rostrally through the sympthetic chain to the heart and/or (c) by central volume depletion with unloading of low pressure receptors, a mechanism which previously has been shown to increase the sensitivity of the high pressure system to blood pressure changes (3). This would indirectly increase the MF variability.

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A.63

QT INTERVAL AFTER ISOFLURANE OR HALOTHANE ADMINISTRATION DURING SURGICAL PROCEDURES

Kanakoudes F, Petrou A, Kalaitzidis A, Konstantinidou A, Michaloudis DG

"THEAGENIO" Hospital, Thessaloniki-GREECE

Prolongation of QT interval may produce hazardous ventricular arrhythmias[1]. Anaesthetics have been involved as cause of QT prolongation[2]. Correlation between plasma catecholamines level and QT interval has also been found[3]. The aim of this study was the possible effects on QTc because of isoflurane (ISOF) or halothane (HALO) adminstration, once the surgical stress had been established.

Fifty consecutive patients ASA I or II, age 52±12 yr and weight 71±11 kg, who were scheduled to undergo laparotomies under general anaesthesia, randomised to receive either ISOF (No 25) or HALO (No 25). Patients with electrolyte imbalance or ECG abnormalities were excluded. Anaesthesia was induced with fentanyl, thiopental, vecuronium and maintained with N_2O and additional doses of fentanyl and vecuronium as required. Fifteen minutes after surgery had commenced, patients were administered ISOF 1% or HALO 1%. ECG recordings for QTc measurements, as well as BP and HR, were taken before induction of anaesthesia (phase 1), just before volatile administration (phase 2), and 10 minutes later (phase 3). ECG recordings were obtained in standard lead II and with paper speed 50 mm/sec.

Blood pressure and heart rate fluctuations were similar in both groups. QTc values (msec) in the phases described are shown in the TABLE.

	Group ISOF	Group HALO
Before induction	424±28	429±32
Before volatile administration	431±35	434±34
10 min volatile administration	435±34*	437±38

(* $p<0.05$ compared with value before induction, t-paired test)

During surgical procedure increasing tendency of the QT interval (but not statistically significant) was found, probably because of insufficient block of stress response despite good clinical signs. The consequent administration of volatile anaesthetic did not further prolonged the QT interval in HALO group, but significantly ($p<0.05$) prolonged it in ISOF group. Mean values of QTc were within normal range.

We believe that, despite the clinically insignificant prolongation of QTc by ISOF, clinicians dealing with patient prone to long QT syndromes should keep in mind this possibility.

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A.64

INTERSTITIAL FLUID VOLUME DURING CARDIAC SURGERY MEASURED BY MEANS OF A NON-INVASIVE CONDUCTIVITY METHOD

C.G. Olthof, P.G.M. Jansen(*), E.R. Bulder, J.J. de Lange, P.M.J.M. de Vries(#)

Departments of Anaesthesiology, Cardiac Surgery(*) and Internal Medicine (#) Free University Hospital, Amsterdam, The Netherlands

Background and goal of study: Interstitial fluid accumulation is frequently found after cardiac surgery. This can lead to pulmonary and myocardial oedema. The origin may be two-fold: a) the noninfectious whole body inflammatory response due to blood contact with the extracorporeal circuit, and b) a change in Starling forces due to a decrease in colloid osmotic pressure (COP) caused by the prime solution of the extracorporeal circuit (ECC). The aim of the study was to determine the influence of haemodilution on changes in interstitial fluid volume (ISFV).

Materials and Method: 11 patients undergoing coronary artery bypass grafting with the use of ECC were studied. ECC was primed with 2000 ml Ringer's lactate, 200 ml human albumin 20%, 50 ml sodium bicarbonate, 100 ml mannitol 10% and heparin 5000 IE. To measure the changes in ISFV a non-invasive conductivity method was used, which was extensively validated under dynamic circumstances [1]. During this study, COP, fluid balance, and ISFV changes were measured.

Results and discussion: During the first minutes of cardiopulmonary bypass (CPB) a steep significant decrease in COP (38.6 ± 6.9 %), and a significant rise in ISFV (5.5 ± 2.8 %) was noticed. After this decrease COP increased significantly, till the end of the operation, but did not reach the pre-operative level (89.5 ± 13.3%). A further increase in ISFV was noticed till the rewarming point (11.9 ± 3.7%). After this point no significant change in ISFV was noticed. Furthermore, a significant correlation was found between the fluid balance and the ISFV increase at all the points of measurement.

Conclusion: it can be concluded that the changes in ISFV are most pronounced during the first part of CPB, probably due to a steep decrease in COP, resulting in a disturbance of the Starling forces across the capillary wall. Furthermore, it can be supposed that the intensity of this disturbance might be an important factor in the development of post-operative pulmonary oedema or post-perfusion syndrome.

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A.65

SAFETY AND EFFECTIVENESS OF AN ORAL PREMEDICATION REGIME BEFORE CARDIAC SURGERY

Bernd W. Böttiger, Helmut Rauch, Rainer Haußmann, Franz Fleischer, Eike Martin

Department of Anaesthesiology, University of Heidelberg, D-69120 Heidelberg, Germany

Background: Decreased oxygen saturation has been reported following intramuscular premedication preceeding cardiac surgery [1-3]. This is associated with the risk of further ischaemia in some patients [3]. We have investigated oral benzodiazepines considering safety, anxiolysis, sedation, and cardiovascular effects.

Methods: With institutional approval informed consent was obtained from 35 patients (ASA II-IV, 21-84yrs, 44-108kg) scheduled for elective coronary artery bypass surgery (n=23) or valve replacement (n=12). They received orally 20mg of the anxiolytic chlorazepat dipotassium (CD) in the evening before surgery (10 p.m.) and 2mg of flunitrazepam (F) 60 min before induction of anaesthesia. If the operation starts after 8.30 a.m., they received an additional 20mg of CD at 6.15 a.m.. Where body weight was less than 50kg or age exceeded 70yrs, dosages were reduced by 50%. Oxygen saturation (SaO_2) was measured (Nellcor N10) the day before surgery and again on reaching the operating room. Before induction, arterial blood pressure (AP) (Dinamap, Critikon), heart rate (HR) and degree of sedation were measured. After insertion of an arterial line, PaO_2, $PaCO_2$, and pH were determined (Ciba-Corning 288). An objective measure of patients anxiety was obtained from the patient (P) using a visual analogous scale (VAS) from 0 (no anxiety) to 10 (greatest anxiety ever) and from the anaesthesiologists viewpoint (A). Statistical analysis was performed using the sign-test (p <0,05 = significant).

Results: The mean SaO_2 was 95,90% (92-100) on the day before surgery and 95,42% (92-98) (p=0,28; n.s.) on reaching the operating room. The other mean values before induction were: PaO_2 77,8mmHg (61,4-100,9)), PCO_2 39,1mmHg (30,8-44,3), pH 7,40 (7,32-7,44), systolic AP 138mmHg (109-181), diastolic AP 76mmHg (51-92), and HR 68bpm (47-99). Most patients (n=21) were considered to be awake but drowsy, 8 patients as asleep but easily rousable, 6 patients were only lightly sedated (4 of these had received their F less than 20 min. before). The mean anxiety VAS decreased from 3,94 (P) and 4,62 (A) on the day before surgery to 3,27 (P; p<0,002) and 3,26 (A; p<0.001) respectively on reaching the operating room.

Discussion: This study shows, that, in contrast to intramuscular premedication regimes, there is no significant decrease of SaO_2 after oral premedication with a combination of CP and F. Reduction of patients anxiety was highly significant (P and A). Nearly all patients were considered to be well sedated.

Conclusion: We conclude, that the combination of anxiolytic CP and more sedating F is a safe and effective oral premedication regime before cardiac surgery.

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A.66

CARDIOPULMONARY BYPASS DURING SINGLE LUNG TRANSPLANTATION AMONG HETEROGENOUS RECIPIENTS

Jose A. Carrera, Leonard Firestone, Susan Firestone, and Jose L Arroyo.
Dept. of Anesthesiology, University Clinic of Navarre, Pamplona, Spain, and Dept. of Anesthesiology/CCM, University of Pittsburgh, Pittsburgh, PA, USA.

Background The principal advantage of single lung transplantation (SLT) is the lack of routine use of cardiopulmonary bypass (CPB). However, some patients are treated with CPB as a consequence of profound hemodynamic and/or respiratory alterations resistant to conventional treatments (1,2). This decision often is made under acute emergency conditions. To improve our ability to predict the need for acute CPB in this setting, we analyzed relevant clinical characteristics associated with CPB in patients undergoing SLT during 2 recent consecutive years at Presbyterian Univ. Hosp., Pittsburgh, PA, USA.

Methods With institutional approval, *all* patients who underwent SLT from January 1991 to January 1993 were studied. The following hemodynamic and respiratory preoperative values were recorded: right and left ventricular ejection fractions (RVEF, LVEF), cardiac index (CI), mean pulmonary arterial pressure (mPAP), transpulmonary gradient (TPG) and the % predicted for FEV_1, FVC and DLCO. Futhermore, the intraoperative changes of P_a0_2 and mPAP were compared before and after anesthesia induction (basal and postinduction), and just after the onset of one-lung ventilation (OLV). The association between the use of CPB and particular attending anesthesiologists and surgeons also were analyzed by Fisher's exact test. Group means and standard deviations of CPB and nonCPB groups were compared by *t test.*

Results Among 55 patients (24 males, 31 females, age range: 17-66 y.o.) who underwent first-time SLT, twenty (36%) were placed on CPB. The diagnoses were: emphysema (3 patients in CPB group vs 27 nonCPB), primary pulmonary hypertension (5 vs 1), Eisenmenger's syndrome (3 vs 0), idiophatic pulmonary fibrosis (3 vs 3), sarcoidosis (4 vs 2), scleroderma (2 vs 0) and lymphangiomyomatosis (0 vs 2). There were no differences in the use of CPB among the various attending anesthesiologists or surgeons. The CPB group had lower RVEF (30±11.3 vs 42±10 for nonCPB group, p<0.001) and CI (2.5±14.8 vs 3.0±0.68, p<0.02) along with higher mPAP (51±20 vs 23±9.9, p<0.001) and TPG (44±22.6 vs 15±8.1, p<0.001). In contrast, the nonCPB group had poorer FEV_1 (62±33.8 for CPB group vs 27±17.7 for nonCPB, p<0.001) and DLCO (58±28.2 vs 35±16.2, p=0.01). However, there were no differences for LVEF and FVC between groups. Intraoperatively, the CPB group had higher mPAP's and lower P_a0_2's at several key intervals. Specifically, mPAP values were significantly higher (p<0.001) in the CPB group at basal (59±23.6 vs 23±6.9), postinduction (56±22.5 vs 29±6.8) and OLV (57±16 vs 30±6.7), while P_a0_2 were lower (p<0.02) after induction (313±193 vs 445±120) and onset of OLV (112±112.2 vs 219±139.1).

Conclusions Pulmonary vascular diseases were strongly related to the use of CPB. However, pathological diagnosis alone does not predict its need. RVEF, CI, and mPAP, but not LVEF, distinguished patients who were placed on CPB during SLT. Preoperative respiratory tests were not as useful, but P_a0_2's proved to be significantly lower in the CPB group after mechanical ventilation was established. The need for CPB among patients with parenchymal diseases arose by mechanical or other factors besides oxygenation and pulmonary vascular pressures.

References 1. De Hoyos AL et al. J Thorac Cardiovasc Surg 1992; 103:295. 2. Hirt SW et al. Ann Thorac Surg 1992; 54:676.

A.67

ENDOTHELIN CLEARANCE BY PULMONARY CIRCULATION IN PATIENTS UNDERGOING AORTOCORONARY BYPASS GRAFTING

J. H. Hähnel, K. H. Lindner, M. Georgieff

Universitätsklinik für Anästhesiologie, Ulm

Goal of the study was to determine whether pulmonary endothelin (ET) clearance from plasma is modified during aortocoronary bypass grafting.
Materials and methods. Eight male routine patients without significant concomitant disease were included in a convenience sample trial. The patients were given a strictly standardized anaesthesia using dopamine as the only catecholamine at a rate of 3.5-5 µg/kg·min. Samples were drawn in rapid sequence from a cannulated radial and a distal pulmonary artery (*via* Swan-Ganz catheter) at eight sampling times starting after induction of anaesthesia and catheter placement until 22 h after the end of operation. ET-levels were determined by a ET-1,2,3 sensitive radioimmunoassay.
Results and discussion. There was a significant ($p<0.05$, two-tailed Wilcoxon-test) extraction of ET by the pulmonary circulation after induction of anaesthesia (1.42±0.96 pg/ml pulm. art. vs. 0.83±0.53 pg/ml rad. art.), which decreased during surgery, but tended to be restored 22 h postoperatively to an approximately twofold increased level (2.55±1.44 pg/ml vs. 1.83±1.33 pg/ml; values are mean ± standard deviation). The previously denied pulmonary ET clearance during aortocoronary bypass grafting [1] is shown to vary perioperatively, depending on the time of sampling.

1. Ray SG, McMurray JJ, Morton JJ, Dargie HJ. Circulating endothelin is not extracted by the pulmonary circulation in man. Chest 1992; 102: 1143-1144.

A.68

EVIDENCE OF SYMPATHETIC CARDIAC REINNERVATION AFTER HEART TRANSPLANTATION IN CHILDREN.

I. Constant MD *, JL Elghozı MD,PhD**
(*) Dpt of Anesthesiology, Hopital Armand Trousseau and (**) Dpt of Clinical Pharmacology, Hopıtal Necker, Paris

INTRODUCTION : Cardiac transplantation implies surgical section of sympathetic and parasympathetic cardiac nerves. In human, most of the studies have failed to demonstrate cardiac reinnervation [1,2], although it has been described in animals [3]. This study was designed to characterize heart rate variability and systolic blood pressure variability patterns in the orthotopic cardiac transplant recipient, a clinical model of denervated heart.
METHODS . After institutional approval, 19 post-transplant subjects (5-16 years) were studied 2 to 74 months after transplantation and matched with 8 healthy control (group C, 5-15 years). All transplanted patients were treated with cyclosporin and azathioprine. Continuous finger blood pressure (BP) and heart rate (HR) were recorded with a non invasive device (Finapres) in 3 positions: standing, supine and tilt. Spectral analysis of SBP and HR was performed to evaluate the autonomic components of short term variabilities. Low frequency (100 mHz) fluctuations (LF) of HR reflect parasympathetic and sympathetic cardiac control, while high frequency fluctuations (HF) of HR reflect parasympathetic neural cardiac control (respiratory arrhythmias). In addition, BP fall and HR rise associated with quick change from supine to standing position were measured to test cardiovascular reactivity. Data were analyzed with ANOVA. Results are mean ± SEM.
RESULTS : In transplant recipients, standard deviations (SD) of HR values were significantly lower than in the control group. Among the former, 2 different profiles of HR were individualized (table):
- group A (n=12): flat HR traces without fluctuations together with no detectable peak in the 100 mHz frequency region were observed in the 3 positions
- group B (n=7): HR traces showed some fluctuations. In addition, a noticeable peak in the 100 mHz frequency region (LF) was observed in both standing and tilt positions but was absent in supine position. All of those patients had been transplanted for more than 44 months .

During quick changes from supine to standing position, HR rise of about 40 bpm was observed in healthy children (group C); it was only of 20 bpm in transplant recipients of group B and no changes were observed in group A (table).
A significant correlation was observed between time from transplantation (TFT) on one hand, and SD of HR in the 3 positions, area of LF peak (AUC LF) and HR rise during changing position on the other hand.

	HR SD bpm	AUC LF %	HR rise bpm	TFT months
A	1.1± .1*	8.6 ± .7*	5.1±2 0*	23.6±5.5
B	2.5±.3*$	22.0±2.0	19 1±2.4*$	59.4±4.6$
C	6.9 ± .3	21.9±2.1	42.2±4.1	-

* p< 0.05 vs C ; $ p<0.05 B vs A

DISCUSSION : This is the first study evidencing clinical signs of cardiac sympathetic reinnervation after heart transplantation in human. Two characteristics of our patients have to be pointed out : first the mean time interval from transplantation to our recordings is greater than in most adult studies; and, second, by contrast to adults, those children were not receiving any cardiac drug known to interfere with autonomic system.
REFERENCES : [1] Schroeder JS. Transplant Proc 11:304-308,1979 [2] Regitz et al. Circulation 82·620-623,1990 [3]Kay et al. Am J Physiol 233:H431-H437,1977.

A.69

EFFECT OF CIRCULATORY SUPPORT WITH THORATEC SYSTEM ON RENAL FUNCTION.

Pérez-Reiner R, Osorio G, Monedero P, Llorens R, Iribarren MJ, Arroyo JL.
Departments of Anesthesiology and Cardiology. University Clinic. Faculty of Medicina. University of Navarre. Spain.

Background and goal of study: The Thoratec system is used for temporary circulatory support in patients with acute cardiac failure pending recovery of the natural heart or a bridge to cardiac transplantation.
The purpose of our study is analized the effects of Thoratec system as a bridge to cardiac transplantation, on diuresis, creatinine clearance (CrC) and fractional excretion of sodium (FENa%) in patients .

Materials and methods: From January 1991, to September 93, a biventricular assist device, Thoratec was implanted as bridge to transplant, in four patients. All of this patients were in preoperative renal dysfunction (CrC < 35 ml/min, Plasma urea (PV) > 2.5 g%).
In all patients were studied CrC, plasma renin activity (PRA), plasma aldosterona (PA) and (FENa), during the first six days after implantation of device.

Results: In these patients a marked improve of CrC > 100 ml/min, PV < 1 g% and FENa > 1%, were observed from the fourth day.
The values of aldosterone were maintained increased during the use of ventricular assistance. The PaO2 was below 70 mm of Hg, (FIO2 0.5).

Conclusion: The results show that a significant increased in cardiac output, due to the mechanical circulatory significant assistance, produces a rapid improving in the parameters of renal function in patients with marked renal dysfunction, in spite of hypoxemia and increased levels of vasoactive substances.

References:

- Pae WE, Pierce WS, Pennock JL et al. (1987) Long-term results of ventricular assist pumping in postcardiotomy cardiogenic shock. J Thorac Cardiovasc Surg 93: 434-441.

A.70

AFTERDROP IN TEMPERATURES AFTER HYPOTHERMIC CARDIOPULMONARY BYPASS.

Agnès Pujol*, Didier Baudouin*, Hervé Lanquetot*, Pierre Ingrand°, Jacques Fusciardi*.

Departments of Anaesthesiology*, Medicale Informatique°, Jean Bernard Hospital and University School of Medicine, 86021 Poitiers, France.

Background and goal of study : After weaning of CPB, a decreases in nasopharyngeal temperature (NPT) occurs (afterdrop). This one is not prevented by extensive CPB rewarming of deep sites, namely rectal or bladder temperatures of 36°C (1) and induces postoperative deleterious consequences (1). The goals of this prospective work were to look for prediction of afterdrop and to study its pathophysiology, which remains unclear.
Materials and methods : We studied 13 sites for monitoring of temperature (noted every 5 minutes) in 8 adult patients during CPB with moderate hypothermia (NPT:28-29°C), and calculated changes in body heat (QBH) during cooling, rewarming, and a 45 min-post CPB period, according to the principe of BURTON (2) and RAMANATHAN (3) involving changes in mean body temperature. This one was estimated taking into account 4 cutaneous temperatures.
Results and discussion : Extended rewarming to 36°C rectal temperature, providing heat gain 1000 ± 65 kJ, (mean ± SEM) equal to CPB-cooling heat loss (-943 ± 87 kJ) did not prevent the afterdrop in core temperature (-1,4°C) and NPT(-1,8°C). Post CPB QBH was -281 kJ ± 32. The afterdrop was not linked to duration of either cooling, or CPB rewarming, or CPB duration. During cooling, the afterdrop was correlated to both the lowest tympanic (fastiest responder) and the lowest deltoid (deep site, mild responder) temperatures ($r=0.76$, $p>0.03$). At terminaison of CPB (end of rewarming) no relationship was found between any single site and the afterdrop. However, the more the difference between the fastiest (tympanic) and the slowest (thigh) sites was, the more pronounced the afterdrop was ($r=-0.667$, $p<0.05$).
Conclusion : The afterdrop is not due to a negative QBH during CPB. It is suggested that, in the post CPB phase, both negative QBH and redistribution of heat from the warmer core to the cooler shell tissues might be involved in the mechanism of afterdrop. This one reflects an heteregeneous distribution of heat during rewarming, between the core and the shell. The monitoring of tympanic temperature during cooling, and of the tympanic-thigh temperature gradient during warming, might be of value in the prevention of afterdrop.
References :

- (1) JOACHIMSON PO, and al. Can J Anaesth 1989 ; 36 : 9-19.
- (2) BURTON A.C. J Nutr 1935 ; 9 : 264-80.
- (3) RAMANATHAN NL. J Appl Physiol 1964 ; 19 : 531-3.

A.71

THROMBOSIS RATE AFTER MITRAL SURGERY. INFLUENCE OF APROTININ

D. EZZARANI*, C. ACAR**, J.-P. COUETIL**,
I. PIPIEN*, M.-Th. COUSIN*

Service d'Anesthésie* et de Chirurgie Cardiaque**,
Hôpital Broussais, 96, rue Didot, 75014 PARIS, FRANCE.

Valvular thrombosis after surgical repair may be a fatal accident. Aprotinin, by improving platelet aggregation impaired during cardiopulmonary bypass (CPB)and by inhibiting thrombus lysis, may be involved in these thrombotic events. The aim of this retrospective study was to examine the clinical thrombo-embolic events (THR E) and the results of echocardiographic studies after mitral valve surgery with or without aprotinin administration.

METHOD

78 patients (pts) underwent mitral valve surgery with the following procedure being performed : mechanical prosthesis, n = 57 ; bioprosthesis, n = 12 ; valvular repair, n = 9. CPB was performed with total hemodilution. Heparin therapy was resumed at 9 ± 3 hours post-op'and changed to oral anticoagulant therapy 3 to 5 days later. Preventive aprotinin was administered in 54 pts (gr A). The control group (gr C) n = 24, did not receive any antifibrinolytic therapy. Thrombosis were sought by echocardiography performed at post op day 7 ± 11.

Small irregular echos (SIE), which may signify a prethrombotic state, were sought in 41 mechanical valvular replacements. Statistical analysis was performed using X^2 test, with significance at $p < 0,05$.

RESULTS (Table I)

Thrombo-embolic events were systemic and were associated in two cases of gr A patients with thrombosis. Thrombosis was observed by echocardiography in mechanical prosthesis replacement but was never obstructive. No thrombi were observed with other procedures.

SIE rate with mechanical prosthesis are shown in Table II. SIE were associated in three cases with thrombo-embolic events, two of which being in gr C.

DISCUSSION

No statistical difference was observed in thrombo-embolic events, thrombosis and SIE rates with respect to patients receiving aprotinin.

SIE which needs, for its identification, a meticulous examination could amplify the undesirable effects of aprotinin. It appears from this study that factors, other than aprotinin, involved in the genesis of thrombosis, remain to be identified.

Table I

	Gr A	Gr C	Total
n	54	24	78
THR E	3 (5,56 %)	2 (8,33 %) NS	5 (6,41 %)
Thrombosis	5 (9,2 %)	3 (12,5 %) NS	8 (10,2 %)

Table II

	Gr A	Gr C	Total
n	30	11	41
SIE	15 (50 %)	5 (45,5 %) NS	20 (48,8 %)

A.72

EARLY POST OPERATIVE MANAGEMENT AFTER CARDIOMYOPLASTY PROCEDURE

I. RATSEP*, D. BENSASSON*, M.-Th. COUSIN*,
J.-C. CHACHQUES**, A. CARPENTIER**

Service d'Anesthésie* et de Chirurgie Cardiaque**,
Hôpital Broussais, 96, rue Didot, 75014 PARIS, FRANCE.

BACKGROUND and GOAL OF THE STUDY

Cardiomyoplasty (CMP) is a surgical technique for improving systolic contraction in refractory heart failure (1). Its benefit is delayed. CMP postop period is thereby critical. The aim of this study is to specify postop evolution and risk factors in CMP surgery.

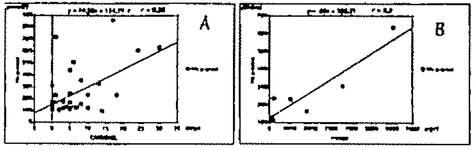
MATERIALS and METHODS

64 patients (pts) (50 ± 13 years), with preop isotopic ejection fraction (EF) 18,1 ± 8,5 % and functional class 3,3 ± 0,5, underwent CMP. In 23 cases CMP was combinated with valvular, coronary or myocardiac resection surgery under cardiopulmonary bypass (CPB). Standard cardiac surgery postop management was systematically completed with anti-staphylococcic therapy and inotropic drugs. In 15 recent cases intra-aortic counterpulsation (IACP) was started before surgery. Continuous SVO_2 (Opticath Abbott) was monitored and, for the last pts, plasma myoglobin levels were measured. Statistical study used Student's t test, $p < 0,05$ as significant.

RESULTS

The average stay in ICU was 8,6 ± 11 days including 5 ± 10 days under mechanical ventilation ; 7 ± 6,7 days catecholamines support and, for 18 pts, 4,7 ± 4 days IACP. The whole postop mortality was 17,2 % and, when preventive IACP was used, 8 %. Main complications occured in 47 % pts (Table). High serum creatine kinase (CK) up to 15000 U/l, with normal CK-MB fractions, reliable to muscle necrosis, were observed. When measured, myoglobin levels, up to 607O µg/l, were correlated with plasma creatinine (p creat) ($r = 0,9$, $p < 0,01$) (Fig. 1B). Catecholamines administration duration also correlated with p creat ($r = 0,55$ $p = 0,001$) (Fig. 1A). SVO_2 decrease was stabilized after the third day.

Fig.1



CONCLUSION

Preop low isotopic EF and high p creat levels are important risk factors. Avoiding, when possible, CPB procedure and preventively managing low cardiac outpout syndrome (LOS) by IACP may improve CMP postoperative outcome.

TABLE. * = $p < 0,05$

	No comp.	LOS	Renal F	Sepsis	Died
n	34	20	4	4	13
Age	49	53	56+	58*	54
EF	19	17	15*	15*	16
p creat µmol	107	136*	152	137	132
CPB %	29	50	75	50	61
SVO_2 D1	60	56	65	52	54
CK D2	3525	3612	4790	4686	3744*
p creat D2	138	223	415*	365	244

REFERENCE

Circulation 1988, 78, suppl. 3, III - 203 - III - 216.

A.73

ENDOLUMINAL PULSE OXIMETRY, A NEW METHOD FOR CONTINUOUS MONITORING OF PERFUSION OF THE GUT.

S.H.M. Nauta, G.J. Scheffer, A.C Vahl, J.J. de Lange,
J.A. Rauwerda

Departments of Anaesthesiology & Vascular Surgery. Free
University Hospital, Amsterdam, the Netherlands

Background and goal of study: Sigmoid ischaemia is a frequent phenomenon during abdominal aortic surgery. With ruptured aneurysms the incidence of persistent postoperative ischaemia increases to 20%. In the case of transmural ischaemia mortality is almost 100% due to sepsis.

Early detection of ischaemia of the gut during the operation is difficult but of extreme importance, since it is possible to treat this ischaemia by surgical or pharmaceutical interventions (repositioning the cross clamp, inducing vasodilatation or increasing blood pressure).

Materials and methods: We developed a method for continuous monitoring the perfusion of the gut. This method is based on pulse oximetry. A reflection pulse oximeter (p.o.)is fixed on a balloon probe. The probe is positioned via the rectum in the sigmoid. After positioning, the balloon is inflated and the p.o. makes contact with the mucosa of the gut and the local oxygen saturation can be measured and a pulse curve appears.

In 8 patients with clinical signs of gut ischaemia the grade of ischaemia was confirmed by endoscopy and the results were compared with our method.

Results and discussion: In 5 of these patients with low grade mucosal ischaemia we were able to detect a pulse curve and a low saturation between 40% and 90%. All these patients fully recovered without surgical intervention. The other 3 patients showed mucosa necrosis during endoscopy which indicates transmural ischaemia.

Of these 3 patients only 1 patient survived. In this particular patient however, despite the endoscopic diagnosis of transmural ischaemia, we were able to measure a pulse curve and oxygen saturation about 43% indicating a vital serosa. No surgical intervention was undertaken and this patient fully recovered.

Conclusion: We conclude that our method is an early and continuous way to detect and monitor ischaemia of the gut and will in the future allow us to intervene in an early phase of this life threatening complication of aortic surgery.

A.74

TITLE: **MEASUREMENTS OF GASTRIC INTRAMUCOSAL PH IN PATIENTS AFTER CARDIAC SURGERY**

AUTHORS: Y. Bekrar MD, D. Schmartz MD, I. Rausin MD, P Van der Linden MD,PhD, JL.Vincent MD,PhD

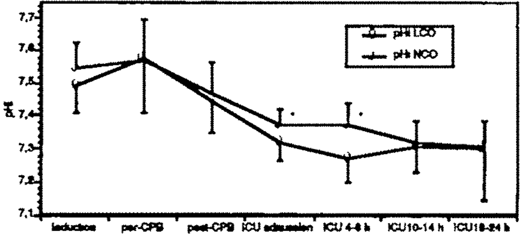
AFFILIATION: Dept of Anesthesiology and Intensive Care, Erasme Univ. Hospital, Free University of Brussels, B-1070 Belgium.

Splanchnic ischemia may be associated with postoperative complications following cardiac surgery. Serial measurements of gastric intramucosal pH (pHi) may represent a valuable tool to assess the adequacy of splanchnic perfusion in these conditions. The aim of our study was to evaluate the time course of pHi in patients after cardiac surgery. Informed consent and institutional approval for the study were obtained.

In 28 patients (40-84 years) undergoing cardiac surgery for coronary artery bypass (N=19) or valve replacement (N=9), pHi was determined together with a complete hemodynamic profile at time of induction of anesthesia, during and after cardiopulmonary bypass (CPB), at ICU admission, and after 4-6 h, 10-12 h, and 18-24 h of ICU stay. pHi was obtained by a nasogastric tonometer (TRIP, Tonometrics, Worcester, MA). Each patient was monitored with a pulmonary artery catheter and an arterial catheter. Anesthesia was obtained with high doses of opiates together with midazolam and pancuronium. The patients were divided into two groups, based on their persistent requirements in inotropic support 24 hours after ICU admission: 7 patients had a low cardiac output requiring the administration of > 5 mcg/kg/min of dobutamine (LCO), and the other 21 patients did not require this adrenergic support (NCO). Data were analyzed by an analysis of variance for repeated measurements (mean ± SD).

During the first hours in the ICU, LCO patients and NCO patients had similar hemodynamic parameters. However, LCO patients had a lower pHi and a higher blood lactate level than the NCO patients. They also had a higher PCO2t measured by tonometry. Mixed venous PCO2 or veno-arterial PCO2 differences were similar (Figure and Table). pHi and blood lactate were significantly correlated (r = 0.65, p <0.001).

Figure



In conclusion, there is a prolonged reduction in pHi in patients after cardiac surgery, which reflects not only the metabolic acidosis but also an increased PCO2 production in the gut mucosa. The reduction in pHi is more profound in the first postoperative hours in the patients with compromised hemodynamic status. Serial measurements of pHi appears to represent an early and valuable indicator of cardiovascular dysfunction following cardiac surgery.

References:

1 Critical Care Medecine 1987; Vol. 15, N° 2; 153-6
2 Chest 1992; Vol.102, N° 2; 135S

A.75

MISOPROSTOL REDUCES GASTRO-DUODENAL LESIONS AFTER CABG SURGERY

C. ISETTA, J. CORALLO*, G. PAOLONI, J. JOURDAN*,
D. GRIMAUD.
Department of Anaesthesiology,
Hôpital ST ROCH, 06006 NICE Cédex
* Department of Cardiac Surgery

Background and goal of the study : Gastroduodenal lesions after coronary bypass grafting (CABG) are represented by mucous erosions or ulcerations wich can have haemorragic manifestations. The frequent prescription of non steroid anti-inflammatory agents after cardiac surgery contributes in aggravating these haemorragic complications. The aim of this open prospective study is to evaluate the frequency of proximal digestive lesions after CABG with ad without an anti-ulcerous, antisecretory and cytoprotective agent, misoprostol which is a synthetic analog of prostaglandme E1.

Materials and methods : Following institutional approval and informed consent, 2 consecutive groups (A and B) of 60 patients scheduled for elective CABG surgery were explored by proximal digestive endoscopy systematically between the 4 th and the 6 th post operative day. Group A patients were not treated by misoprostol , group B patients received 2 days before operation and the following postoperative days 200 mcg twice daily of misoprostol. Gastroduodenal lesions were classified as has been described by Lanza (1). Statistical studies used analysis of variance and Student's t-test considering a p<0,05 as significative

Results and discussion : The two groups were homogeneous with regard to their make-up and CPB parameters (table I). Quality and importance of lesions were significantly different in the two groups (table II). In group A the number of patients with gastric and duodenal lesions was greater (40 patients, 66%) than in group B (28 patients, 45 %; p<0.05), specially for duodenal lesions. The association of gastric and duodenal lesions in the same patient was higher in group A (5 patients) than in group B (2 patients).

Conclusion : Pre and postoperative treatment by misoprostol reduces significantly gastro-duodenal lesions after elective CABG surgery with CPB.

Référence : 1. N Engl J Med 303 : 136-138, 1980

TABLE 1	**A** (n= 60)	**B** (n = 60)
age years	64 + 9	64 + 8
sex ratio (M/F)	52/8	53/7
weight (kg)	73 + 14	70 + 11
bypass (n)	3 +1	3 + 1
CPB time (min)	94 + 26	93 + 29

TABLE 2	**A** (n = 60)	**B** (n= 60)
gastric lesions	8	3
grade 1	3	1
grade 2	4	1
grade 3	1	1
grade 4	0	0
duodenal lesions	37	27 **
grade 1	10	9
grade 2	11	8
grade 3	10	4
grade 4	6	6

** : p<0.01

A.76

Jugular bulb venous oximetry and cerebral blood flow in fentanyl/isoflurane anaesthetised patients.

Algotsson L.
Department of Anaesthesiology, University Hospital, Lund, Sweden.

Background: There is an increasing world-wide experience in the use of oxygen saturation of haemoglobin in jugular bulb blood for monitoring head injured patients and patients undergoing cardiac surgery or carotid endarterectomy. Low jugular venous bulb oxygen saturation (SjO_2) provides information on cerebral hypoperfusion as a result of either hypotension or low cerebral blood flow (CBF) or both. CBF relates to the cerebral metabolic rate for oxygen ($CMRO_2$) and arterial venous difference for oxygen ($AjDO_2$). If $CMRO_2$, haemoglobin and oxygenation are unchanged the SjO_2 could be a direct monitor of CBF. The present study was performed to evaluate the relation between CBF and SjO_2 during hyper- and normoventilation.

Materials and Methods: Eleven patients (9 women, 2 men; mean age 47 years) without cardiovascular or pulmonary disease undergoing cholecystectomy were investigated. After induction of anaesthesia with thiopentone, anaesthesia was maintained with fentanyl/isoflurane in N_2O/O_2 or O_2/air. MAC for inhaled anaesthetics were 1.3. All patients where mechanically ventilated. CBF was determined after intravenous administration of ^{133}Xenon. Clearance of the tracer was measured with two scintillation detectors positioned over both parieto-temporal regions and from expired air. One catheter in the radial artery and one in the jugular vein with its tip at the bulb were used for intermittent arterial and venous blood sampling. Determination of CBF, haemoglobin, blood gases, oxygen content and oxygen saturation were performed twice in each patient. Seven of the patients were examined during normoventilation and five during hyperventilation.

Results: Mean arterial blood pressure and the estimated $CMRO_2$ were not different between the two groups. During normocapnic conditions ($PaCO_2 > 4$ kPa) there was a positive correlation between CBF and SjO_2 ($r=0.81$, $2p<0.002$). There was no correlation between the two parameters during hyperventilation ($PaCO_2 < 4$ kPa).

Conclusion: Using SjO_2 as a measure of CBF in situations where hypoperfusion may exist, seems valid during normocapnic conditions. In hyperventilated patients SjO_2 does not relate directly to CBF. This is important in the care of patients with impaired cerebral perfusion after severe brain injury and intraoperatively during carotid or cerebral vascular surgery.

A.77

Effect of pentoxyfillyne on oxygen transport during aortic reconstruction (preliminary report)

Pasquale Piccinni, Antonino Tripepi, Leonardo Meneghetti
Liliana Lora*, Diego Martines*

Servizio di Anestesia e Rianimazione, *Gastroenterologia,
Universita' di Padova, 35100 Padova, Italy

Background and goal of study: It is hypothesized that pentoxifylline may be beneficial during shock states by improving tissue oxygenation (1). To test this hypothesis, we examined the effect of pentoxifylline on hemodynamics, oxygen delivery(DO2) and tissue metabolism during reconstructive aortic surgery.

Materials and Methods: We performed a complete hemodynamic study in ten adult patients who underwent elective aortic reconstruction whith constant temperature, stable hemoglobin levels during homogeneous anaesthesiological and technical procedures, which included also venous-venous bypass. We used a thermodilution fiberoptic pulmonary artery catheter (Swan-Ganz-Abbott) and a Oximetrix 3 computer which provided continuous measurements of venous oxygen saturation (Svo2) and thereby enabled us to calculate VO2I, DO2, O2Ex, SVRI.. Hemodynamic profiles were determined after anaesthetic induction (basal, 1), 15 minutes after aortic clamping (2) and 15-30 minutes after declamping (3, 4), Five patients were treated with a 10mg/kg bolus of iv pentoxifylline started at clamping and followed by a continuous infusion at 5mg/kg./hr. The controls consisted of five patients untreated.. Samples of arterial blood were taken simultaneously for TNF, hemoglobin blood concentration and arterial oxygen saturation.

Results and discussion: Repeated measurements of the control and pentoxifylline groups showed significant differences in cardiac output, systemic vascular resistences, O2 delivery and O2 extraction who improved in Pentoxifylline group ($p<0,02$ t-Student's for paired data) but non in TNF concentration.

Conclusion: Pentoxifylline increase microcirculatory flow through underperfused capillary beds by decreasing cardiac afterload. Further studies of effects on vascular endothelial damage are warranted.

Reference: 1).Soliman HM, O'Neal K, Waxman K: Pentoxifylline improves tissue oxygenation following anesthesia and operation. Crit Care Med 1987;15:93

A.78

INFLUENCE OF MODE OF WEANING ON POSTOPERATIVE MYOCARDIAL ISCHEMIA

Droc G., Phillipe E., Pansard J.L, Ouis N.,
Coriat P, Viars P.
Département d'Anesthésie-Réanimation, G.H. Pitié-Salpêtrière, 75651 Paris Cédex 13, France

In patients undergoing aortic surgery, the highest incidence of myocardial ischemia (MI) occurs postoperatively. Weaning from mechanical ventilation, which increased whole body oxygen consumption, may be a causative factor for postoperative MI, the deleterious effect of which have been firmly established (1).

The aim of this study is to determine whether the mode of weaning influences the incidence of MI following aortic surgery.

Methods : 69 patients, meeting standard extubation criteria following abdominal aortic reconstruction, were randomised into two different modes of weaning : T piece breathing room air supplemented with 02 (group T n = 34) or pressure support ventilation (PSV) set at 15 cmH_2O (group PSV n = 35). Heart rate (HR), mean arterial pressure (MAP), mean pulmonary arterial pressure and oxygen arterial saturation were continuously measured 45 minutes before, during weaning trial (45 min.) and 45 min after extubation Throughout the study period MI was detected using a continuous 3 lead ST segment analyser (Merlin, Hewlett Packard) . Ischemia was defined as 1 mm ST segment depression 60 m/sec after the J point.

Results : Hemodynamic variables were similar in the 2 groups before the weaning trial and after extubation.

During the weaning trial 12 ischemic episodes occurred in 9 patients in group T (mean ischemic time per patient : 22 ± 3 min). By contrast only 3 ischemic episodes were noted in 2 patients in group PSV ($p < 0,01$). The highest MAPxHR product noted during the weaning trial was significantly higher in group T (10242 ± 2600 vs 8560 ± 2090 b.min.mmHg $p < 0,005$).

Conclusion : Standard postoperative weaning from mechanical ventilation is associated with a high incidence of myocardial ischemia By contrast PSV limited the myocardial stress response of the weaning period and thus reduced effectively the incidence of postoperative MI.

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A.79

HEMODYNAMIC AND HUMORAL EFFECTS OF SIMULTANEOUS AORTIC AND INFERIOR VENA CAVA CLAMPING DURING TOTAL ABDOMINAL ISCHEMIC PERFUSION.

H. Berkenstadt, A. Perel, N. Lieberman, E. Peleg, E. Klein, G. Ben-Ari.
Depts of Anesthesiology and Surgery, (Sackler school of Medicine, Tel Aviv University) Sheba Medical Center, Tel Hashomer, 52621, Israel.

Previous animal studies concluded that the hemodynamic changes induced by aortic cross clamping (Acl) are prevented by simultaneous inferior vena cava clamping (Vcl) (1,2). We have recently studied this issue in patients undergoing Total Abdominal Ischemic Perfusion for inoperable intraabdominal malignancy.
During the procedure the abdominal organs are being perfused with cytotoxic agents and isolated from the systemic circulation by simultaneous baloon occlusions of the lower thoracic aorta and vena cava.
Hemodynamic data were measured in ten patients at baseline (BL), after isolated Vcl, after Acl and after simultaneous Acl and Vcl (AVcl). Volume replacement and drug infusions were adjusted according to clinical needs.
Isolated Vcl and Acl produced significant hemodynamic changes that are shown in the table. When Vcl was added to Acl (AVcl) no further hemodynamic changes occured. Plasma norepinephrine levels did not change during Acl (491±400pg/ml before and 327±159 after Acl) or following AVcl (373±282), but increased after AV declamping (596±377 , p<.05).

	BL	Vcl	BL	Acl	AVcl
BP	79±13	62±16*	78±11	105±16*	106±21
HR	69±8	69±7	68±6	59±6*	63±7
$ETCO_2$	29±3	25±6*	29±4	26±4*	24±5*
CVP	11±4	8±5	13±4	16±5	13±4
PAP	18±5	12±3*	19±6	22±5*	19±5
PCWP	12±3	10±5*	13±4	18±4*	15±4*
CO (dl/min)	49±7	37±15*	55±10	35±8*	34±5

*=p<.05 (compared to previous measurement)

We conclude that Vcl alone may cause reduction in filling pressures and cardiac output. However, when Vcl is added to Acl it does not affect the hemodynamic changes induced by Acl except for a slight reduction in PCWP. These latter findings are in contrast to previous studies which claim that Vcl prevents the hypertension that is normally associated with Acl, by reducing preload (2) or by blocking the entrance of metabolites from the ischemic abdominal viscera into the systemic circulation(3).

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A.80

Ultrasound delivered energy to the heart does not affect central hemodynamics, coronary vascular dimensions or coronary morphology.

Algotsson L[a], Höyer S[b], Lyttkens K[c], Nilsson AM[d], Roijer A[d], Olsson B[d]. Departments of Anesthesiology[a], Clinical Radiology[c] and Cardiology[d], University Hospital, Lund, Sweden. Department of Pathology[b], Rigshospitalet, Copenhagen, Denmark.

Background: Transesophageal echcardiography (TEE) is an excellent guidance for maintenance of cardiovascular stability during surgical procedures. However, ultrasound of moderate intensity accelerates streptokinase-induced thrombolysis under experimental conditions[1]. The present study aims to elucidate effects of ultrasound delivered energy to the heart on coronary vascular morphology and central hemodynamics.

Materials and methods: 8 pigs (20-25 kg) were anesthetized with ketamine-pancuronium. A Swan-Ganz catheter was introduced from the external jugular vein to the pulmonary artery and an arterial catheter was placed in the carotid artery. The heart was exposed by median sternotomy. A 6 F Judkins coronary catheter was introduced from a femoral artery and advanced to the left coronary ostium. Thereafter an ultrasound transmitter was positioned over the middle part of the left anterior descending coronary artery. Before and after 0.5, 1.0 and 2.0 W/cm^2 (SATA; spatial average temporal average) 1 MHz continuous ultrasound exposure, each for 5 minutes, heart rate, mean arterial blood pressure (MAP), cardiac output (CO), pulmonary capillary wedge pressure (PCWP) and oxygen consumption (VO_2) were recorded and angiography of the left coronary artery was performed. Thereafter the heart was prepared for microscopic analysis.

Results and discussion: Ultrasound exposure of the left descending coronary artery did not induce any significant changes of central hemodynamics or oxygen consumption. No angiographic changes of the vascular diameter were noted, nor were any morphological changes of the coronary artery seen on microscopic investigation. As the ultrasound energy delivered to the coronary artery in the present study was about 100 times the energy delivered during TEE, it is assumed that TEE monitoring, even long-term, does not affect heart function and coronary circulation.

Conclusion: We conclude that ultrasound of the intensity and profile delivered during TEE, is not accompanied by any undesirable effects on cardiac function, coronary diameter or morphology. This is also true for ultrasound delivered energy which can accelerate a thrombolytic process in the pig.

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A.81

EFFECTS OF MILRINONE, SODIUM NITROPRUSSIDE AND ISOFLURANE ON CARDIOVASCULAR RESPONSES TO EXPERIMENTAL ABDOMINAL AORTIC CROSS-CLAMPING.

Seeman-Lodding H, Biber B, Martner J, Pontén J and Winsö O.

Department of Anesthesiology and Intensive care,
University of Gothenburg, Östra Hospital,
416 85 Gothenburg, Sweden.

AIM: To study the efficacy of the PDE III inhibitor milrinone (MIL) vs. isoflurane (ISO) or sodium nitroprusside (SNP) for control of blood pressure augmentations during experimental infra-renal aortic cross-clamping (AXC).

METHODS: Mean arterial pressure (MAP), cardiac output (CO), heart rate (HR), pulmonary artery occlusion pressure (PAOP) and central venous pressure (CVP) were measured in pigs (n=10). Systemic (SVR) and pulmonary (PVR) vascular resistances and systemic oxygen consumption were derived. All animals were exposed to AXC during control (no vasoactive drugs) and during the administration of each of the drugs ISO (0.7%; 1.4%), SNP (5 or 10 µg/kg/min) or MIL (25, 50 and 100 µg/kg).

RESULTS: During control, AXC increased MAP and SVR, but induced no significant changes in CO or HR. Increases in MAP and SVR were not altered by 0.7% ISO or SNP, but attenuated by 1.4% ISO. MIL did not significantly influence the increase in MAP, but at 50 µg/kg attenuated the SVR increase. With SNP, MIL and 0.7% ISO, peak MAP levels *during AXC* were not significantly different, and with 1.4% ISO decreased, from MAP levels during *non-clamped* control. Oxygen uptake during AXC was higher with MIL and SNP than with ISO.

CONCLUSIONS: The objective that MAP during AXC should not exceed levels observed at non-clamped conditions, was effectively obtained by either ISO, SNP or MIL. However, this reflects a different cardiovascular mode of action for each drug. For ISO, the MAP attenuation was produced at the price of pronounced cardiodepression, particularly at the 1.4% dose. SNP, besides producing vasodilation, also significantly increased HR. MIL decreased SVR and produced augmentations in both HR and CO. The differences between the three drugs in terms of effects on oxygen uptake during AXC could be attributable to dissimilar actions on cardiac metabolism.

A.82

THE SYSTOLIC PRESSURE VARIATION REFLECTS LEFT VENTRICULAR END-DIASTOLIC VOLUME (LVEDV) DURING GRADED HEMORRHAGE IN PIGS.

Preisman S, DeSegni E, Vered Z, Shneider A, Perel A.
Department of Anesthesiology and Institute of Cardiology, Sheba Medical Center [Sackler School of Medicine, Tel Aviv University], Tel Hashomer, Israel, 52621.

Background and goals of the study: The systolic pressure variation (SPV) is the difference between the maximal and minimal values of systolic blood pressure (SBP) during one mechanical breath cycle, while the dDOWN (delta DOWN) is the decrease in the SBP relative to the SBP during apnea (1). Both parameters were shown to be able to reflect preload in various clinical and experimental conditions (1-3). We have tested this hypothesis by means of echocardiographic estimation of LVEDV, which is the accepted gold standard of LV preload evaluation, in a model of graded hemorrhage in pigs.

Materials and methods: Seven anesthetized and ventilated pigs were bled by increments of 3-4 ml/kg up to total blood loss of 20 ml/kg. The shed blood was then re transfused and animals were loaded with 10 ml/kg of plasma expander. Measurements were made at each point of the experiment. The SPV and dDOWN were measured from the computer-recorded trace of the blood pressure waveform. LVEDV was calculated according to the bullet formula after the measurement of LV end-diastolic length and area on 2D long-axis and short-axis parasternal views. In addition, central venous (CVP) and wedge (WP) pressures and thermodilution cardiac output were measured at each point, with the calculation of stroke volume index (SVI).

Results and discussion: WP, SPV and dDOWN showed similar r-values for correlation with LVEDV (0 64, -0.62 and -0.67, respectively) However, the correlation of the SPV and dDOWN with the SVI ($r=-0.73$ and $r=-0.78$) was better than that of the CVP ($r=0.30$) or WP ($r=0.34$).

We conclude that in this model of graded hemorrhage the parameters of arterial pressure waveform analysis (SPV and dDOWN) reflect the response of the LV output to the changes in intravascular volume better than the WP and CVP. The SPV and dDOWN reflect LVEDV, obviating the need for more invasive monitoring in the setting of graded hemorrhage and retransfusion.

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A.83

Involvement of Na-Ca exchanger in the positive inotropic effect of hypertonic saline. In vitro study in a blood-perfused isolated heart preparation.

G. Mion, R. Souktani, F. Ouardani, S. Mouren, J.F. Baron[1], S. Dreux, P. Viars.
Department of Anaesthesiology, Hôpital Pitié-Salpétrière, Paris, France.
1. Department of Anaesthesiology. Hôpital Broussais, Paris, France.

Introduction: A positive inotropic effects is demonstrated with hypertonic saline (HS) in various experimental models (1,2). Since intracellular sodium concentration ([Na]i) increases with hypertonic saline infusion (3), a calcium influx through the Na-Ca exchanger working in the reverse mode could mediated this increase in myocardial contractility. Our study compares the myocardial performances of ten isolated rabbits hearts during HS infusion with and without amiloride (A), a Na-Ca exchanger inhibitor .

Methods: Reconstitued blood with red blood cells and modified Krebs-Henseleit buffer was oxygenated and equilibrated to achieve normal acid-base balance. After aortic canulation, the heart was perfused using the Langendorff technique at a constant perfusion pressure. Thus, variations in CBF reflected variations in coronary resistances. Heart rate was maintained constant with an atrial pacing. A cannulated fluid-filled balloon was inserted in the left ventricule (LV) to maintain constant LV volume and to monitor LV pressures. Maximal positive and negative LV pressure derivatives reflected respectively myocardial contractility (dP/dt max) and relaxation (dP/dt min). After baseline measurements with control perfusate ([Na] 140mM), hypertonic perfusate ([Na] 160mM) was infused. Then, [Na] 140mM was infused again and the same protocol was conducted while a continuous infusion of A (0.3 mM) was started . Additionnal experiments performed with sucrose were conducted to evaluate the effects of the same variation of osmolarity without variations of [Na]. Results are expressed as pourcentages of variation. Statistical analysis used a paired t-test.

Results: A positive inotropic effect and a coronary vasodilation were observed with [Na] 160 mM During A infusion, [Na] 160 mM still demonstrated a vasodilating effect but the positive inotropic effect previously reported was abolished. Yet, the inotropic effect of sucrose (ΔdP/dt= +19±7%) was not influenced by A (ΔdP/dt= +24±8%).

Conclusion: The coronary vasodilation and positive inotropic effects of HS is confirmed in this study. A calcium influx through Na-Ca exchange may be involved in the observed positive inotropic effect. The improvement of myocardial performances by hypertonic non ionic solutions is not influenced by A, suggesting a specific mechanism for HS.

	160mM	160mM +Amiloride
Δ CBF %	26 ± 17	59 ± 21*
Δ dP/dt max %	14 ± 6	3 ± 5% **
Measured Na mmol/l	160 ± 3	160 ± 2
Measured Osmolarity mOsm/l	313 ± 9	314 ± 4

* p<0.01, ** p<0.001 vs Na 160

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A.84

INFLUENCE OF CHEMICAL STRUCTURE OF HYDROXYETHYLSTARCH ON ONCOTIC FUNCTION OF PLASMA.

Vogt,N.; Schönfeld,A.; Weigand,M.; Georgieff,M.

Clinic for Anesthesiology, University of 7900 ULM,
Steinhövelstr. 9, Germany

Colloid osmotic pressure in plasma (COP i.p.) regulates intra- extravascular fluidshifts with great influence on plasmavolume and interstitiell fluid content. Hydroxyethylstarch (HES) exerts peculiar effects on plasma oncotic function. HES solutions are physicochemically characterized by concentration (C), molecular weight averages (Mw) and the degree of substitution (DS) with hydroxyethyl groups. It was our intention to examine the invivo influence of Mw and DS of HES on oncotic properties of plasma.

Method: We investigated 40 pigs (weight 24 - 26 kg) under general anesthesia, randomized into 4 groups with 10 animals in each group. After rapid withdrawal of blood (20 ml/kg bodyweight(bw)) and bolus HES infusion (25 ml/kg bw) we infused continuously 3 ml/kg bw/h of HES solution during our study period of 6h. Group 1 consisted of control animals without bleeding, group 2 received HES Mw 200000, DS 0.5 and C 6% (200,0.5,6%), group 3 HES 200,0.62,6% and group 4 HES 100,0.5,6%. 30, 60, 120, 180, 240, 300, and 360 minutes after baseline we measured TSP and COP (oncometer: membrane exclusion range 20000 Dalton). We calculated median values and compared all 3 therapy groups with control group at $p<0.05$ applying multiple Wilcoxontest.

Results: During the whole therapy period a significant but corresponding decrease of TSP between control(1) and therapy groups(2,3,4) appeared, indicating the comparable extent of hemodilution between these 3 groups.

COP LP [mm Hg]	0'	30'	60'	120'	180'	240'	300'	360'
1.Control	12,85	12,9	12,2	12,1	11,9	11,3	11,3	10,7
2.HES 200/0.5 6%	13,95	13,4	12	11	10,8	10,7	10,35	10,2
3 HES 200/0.62 6%	14,5	15,1 *	14,05	13,8	13,6	13,2	12,7	12,55
4.HES 100/0.5 6%	12,8	10,43*	9,55*	8,85*	8,7*	8,6*	8,85*	8,45*

*) P<0.05 Therapy- vs. Controlgroup

Discussion: When examining HES with identical HES concentrations and quantities using our animal infusion model, we conclude that oncotic function is more influenced by the average molecular weight than by the degree of substitution of HES solutions.

A.85

ATRACURIUM INDUCED VASODILATATION IS NOT MEDIATED BY HISTAMINE IN THE ISOLATED RABBIT FEMORAL ARTERY

Diana de Jong, Nico Hoogerwerf, Gert-Jan Scheffer, Jaap de Lange en Pieter Sipkema.

Dept. of Anaesthesiology, Free University Hospital,
Amsterdam, The Netherlands

Background and goal of study: Atracurium (A) causes a decrease of systemic vascular resistance and arterial blood pressure which have been ascribed to histamine release. Histamine (H) receptor blockade however does not prevent these decreases completely. Because of the many interactions in vivo, we studied this aspect in vitro. The effects of H and A on the vasoactive state of the isolated rabbit femoral artery were studied to test the hypothesis that the hypotensive side effects of A are not only due to H release. We also investigated whether vasodilatation caused by A was dependent on the presence of endothelial cells.

Material and methods: Isolated, Tyrode perfused, rabbit femoral arteries were constricted with norepinephrine to about 70% of their resting diameter. Endothelial function was checked with acetylcholine.
After H ($5.0 \cdot 10^{-7}$ or $1.0 \cdot 10^{-6}$ M = H.1) and A (40 $mg.l^{-1}$) were administered, the vessels were divided into three groups. In group one(n=6), H was given on top of H.1 (resulting in a total concentration of 2.0 - $5.0 \cdot 10^{-6}$ M). Thereafter A was given on top of H.1. In group two (n=5), the H and A responses were determined during H receptor blockade. In group three (n=5), the diameter responses to H and A before and after endothelium removal were compared. Finally, some vessel segments (n=5) were prepared for histological examination and searched for mast cells.

Results and discussion: H produced constriction, whereas A produced dilation. The diameter responses to A alone and to A on top of H were not significantly different. Likewise, the responses to A alone and during receptor blockade were not different. Removal of endothelium caused an increase in constriction after H administration, while the response to A remained constant.

Conclusion: We conclude that in the isolated rabbit femoral artery, there is no interaction between the vasoactive effects of histamine and atracurium and that atracurium induced vasodilatation is not histamine or endothelium dependent.

A.86

DISSOCIATION OF SYSTOLIC AND DIASTOLIC FUNCTION DURING ACUTE INCREASES IN CORONARY PERFUSION PRESSURE

W Schlack MD, S Schäfer* MD

Institut für Physiologie and *Klinik für Kardiologie,
Heinrich-Heine-Universität Düsseldorf,
D-40001 Düsseldorf, FRG

Background & goal of the study: Left ventricular (LV) contractile function has been shown to improve during acute increases in coronary perfusion pressure (CPP), long known as Gregg[1] or garden hose effect.[2] The effect of acute increases of CPP on relaxation has not been investigated so far. The aim of the present study was to analyse diastolic function and its relation to systolic function during acute increases in CPP in comparison to the effects of ß-adrenergic stimulation.
Materials & methods: Maximal velocity of LV pressure rise, (+)dP/dt, as an index of myocardial systolic performance and the time constant of left ventricular pressure decline, τ, as a measure of myocardial relaxation were determined in isolated, buffer perfused isovolumically (LV balloon) beating guinea pig hearts. Myocardial oxygen consumption was calculated according to the Fick principle. In eight hearts myocardial function was varied by changing CPP between 60 and 110 cmH_2O in a randomized order. Five control hearts received increasing doses of isoprenaline up to 3.2 nmol/l.
Results & discussion: Inotropic stimulation with isoprenaline dose dependently improved both systolic ((+)dP/dt from 1494(SEM156) mmHg/s by 72(14)%) and diastolic function (τ shortened from 26.3(2.6) ms by 36(4) %). VO_2 increased from 76.5(13) µl/min/g by 64(19)%, all $p<0.05$. Increasing CPP from 60 to 110 cmH_2O only improved systolic function ((+)dP/dt by 47(17)) accompanied by an increase in VO_2 (by 40(42)%, both $p<0.05$). Diastolic function remained unchanged during increases of CPP (τ was 23.6(2.7) at 60 and 22.2(1.7) at 110cmH_2O. While there was a good correlation between contractility ((+)dP7dt) and CPP (r=0.71, p=0.05, n=124) there was no such correlation between τ and CPP.
Conclusions: While an increase in ß-adrenergic tone improves both systolic and diastolic function, acute increases in CPP improve systolic function alone. This leads to a dissociation of systolic and diastolic function. This mechanism may contribute to the impaired LV relaxation process when CPP increases abruptly in an in vivo situation, as observed in hypertensive crisis.

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A.87

ALTERATION OF VENTRICULAR FUNCTION AFTER STELLATE GANGLION BLOCK

W Schlack MD, S Schäfer MD, V Thämer MD

Institut für Physiologie, Heinrich-Heine-Universität Düsseldorf, D-40001 Düsseldorf, FRG

Background & goal of the study: A cervicothoracic sympathetic (or stellate ganglion) block (SGB) with local anaesthetics is an established method in diagnosis and treatment of chronic pain. SGB also leads to a acute sympathetic denervation of a part of the left ventricular (LV) wall innervated by the blocked ganglion. This may impair regional myocardial function. We tested the hypothesis that a left sided SGB results in an imbalance of myocardial contractility between different LV regions which, in turn, may adversely affect LV function by increasing LV asynchrony.

Materials & methods: Six anaesthetized open chest dogs were instrumented for measurement of aortic and LV pressure (tip manometers), cardiac output (CO, thermodilution), and regional LV wall thickness (WT, sonomicrometry) in the anteroapical wall (innervated by right stellate ganglion) and posterobasal wall (left stellate ganglion). A brief occlusion of the inferior vena cava generated LV pressure-wall-thickness loops for calculation of preload recruitable stroke work[1] (PRSW). Contractility of both regions was assessed by the load independent PRSW versus end-diastolic WT relationship (M_W). Timing of regional myocardial contraction was evaluated by the phase of the first Fourier transform of the WT signals, LV asynchrony by the phase difference (PD) between both regions[2], and LV diastolic function by the time constant of isovolumic relaxation (τ). Heart rate was kept constant by atrial pacing and measurements were performed before and after a left SGB.

Results & discussion: MAP decreased from 111 ±22 (mean ±SD) to 90 ±9 mmHg while CO remained stable after SGB (3.25 ±1 to 3.20 ±1 l/min), indicating a decrease of systemic vascular resistance. SGB significantly reduced contractility in the posterobasal myocardium (M_W -170 ±22 to -81 ±8 mmhg, $p<0.01$) accompanied by a regional delay of systolic contraction in this wall (phase 200 ±19 to 222 ±18°, $p<0.05$). This increased myocardial asynchrony (PD 16 ±8 to 38 ±12°, $p<0.01$), and in parallel impaired LV diastolic function (τ 26 ±3 to 32 ±3 ms, $p<0.05$). Anteroapical wall function did not change.

Conclusion: SGB reduces regional contractility of the myocardium innervated by the blocked ganglion. This increases myocardial asynchrony and as a result also impairs diastolic function. These findings may be relevant in patients with compromised hearts in whom LV function depends in part on a high sympathetic tone.

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A.88

EFFECTS OF PROPOFOL AND THIOPENTONE ON LOAD DEPENDENT AND INDEPENDENT INDICES OF LEFT VENTRICULAR (LV) CONTRACTILITY.

M Tugrul, G Johansson, S Häggmark, S Reiz

From the Department of Cardiothoracic Anesthesia & Surgery, University of Umeå, Umeå, Sweden.

Background & goal of study: There is controversy as to the negative inotropic effect of propofol (1). This study examines the influence of propofol vs thiopentone on several indices of LV contractility.

Materials & methods: Ten pigs were subjected to continuous iv pentobarbitone sedation and mechanical ventilation to normocapnia and normoxia. A conductance catheter (2) and a tip manometer catheter were placed in the LV for derivation of pressure volume loops and dP/dT. Arterial pressure was measured in the ascending aorta. After autonomic blockade by iv hexamethonium and methylscopolamine, propofol and thiopentone were administered iv as continuous infusions according to a randomized, cross-over protocol. Each drug was given in two doses, titrated to reduce MAP to stable levels 10-15% and 20-25% below control values. Time between drugs was 2 hours.

Results: Complete data during propofol were collected in all 10 animals, whereas 9 generated complete data during thiopentone infusion. Exclusions were due to technical problems. Control values before each drug were comparable. Results are summarized in the table.

Table: Percent change of mean (SD) arterial pressure (MAP), arterial elastance (Ees), LV stroke work (SW), dP/dT, and the slope of the preload recruitable stroke work (PRSW) vs LV end-diastolic volume (EDV).

		Propofol	*Thiopentone*	*Level of sign.*
MAP	*I*	-13(3)***	-13(3)***	n.s.
	II	-24(4)***	-25(5)***	n.s.
SW	*I*	-14(8)**	-25(15)**	n.s.
	II	-22(16)*	-38(8)***	p=0.01
dP/dT	*I*	-15(11)**	-28(8)***	p=0.01
	II	-26(12)***	-44(11)***	p=0.0043
Ees	*I*	-9(12)*	-10(13)	n.s.
	II	-17(8)***	-18(14)*	n.s.
PRSW	*I*	13(36)	19(64)	n.s.
vs EDV	*II*	17(64)	12(60)	n.s.

I/II - after dose I and II, * $p<0.05$, ** $p<0.01$, *** $p<0.001$ compared to control. Results are means±SD, n=7 (P), n=10 (T).

Discussion & conclusion: Load dependent indices of LV contractility indicated that thiopentone would produce greater cardiodepression than propofol at identical MAP levels. In contrast, the load independent indices represented by the elastance (Ees) and by the slope of the preload recruitable stroke work plotted versus LV end-diastolic volume did now show any difference between the drugs. The results suggests that both drugs produced cardiodepression of the same degree in a pig model subjected to pentobarbitone sedation.

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A.89

PEEP INDUCES AN INDEPENDENT CONSTRAINT ON THE RIGHT ATRIUM AND VENTRICLE

S. Beloucif, M.D$^{\$}$., M.Takata, M.D.*, M. Shimada, D.D.S., and J.L. Robotham, M.D.
Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, MD 21205, *Pathophysiology Research, Children's Medical Research Center, Tokyo 154, Japan and $^{\$}$DAR Lariboisière hospital, Paris.

Introduction : Direct cardiac compression by the lungs is one mechanism for the decrease in venous return during ventilation with PEEP. Atrial pressure waveforms and patterns of vena caval flows into the right atrium during systole and diastole are different during tamponade and constrictive pericarditis. These differences can be explained by uniform atrial and ventricular constraint with tamponade but locally independent constraint with pericarditis. We hypothesized that PEEP would act more like constrictive pericarditis than tamponade.
Methods : Right atrial pressure (Pra) and superior (SVC) and inferior (IVC) vena caval flows were measured with ultrasound transit time probes in 6 anesthetized closed chest dogs. Systolic and diastolic inflow volumes per beat in the SVC and IVC were obtained by integration at baseline and following graded levels of PEEP (0, 10, 15 and 20 cmH_2O). A ratio was calculated and ANOVA with Scheffe's tests performed.

Results:Diastolic/systolic inflow volumes (x ± SE;*P<.05)

PEEP	0 cmH_2O	10 cmH_2O	15 cmH_2O	20 cmH_2O
SVC	0.74 ± 0.13	1.22 ± 0.29	1.62 ± 0.38*	1.57 ± 0.37*
IVC	1.06 ± 0.21	1.52 ± 0.24	1.88 ± 0.30	2.09 ± 0.42*

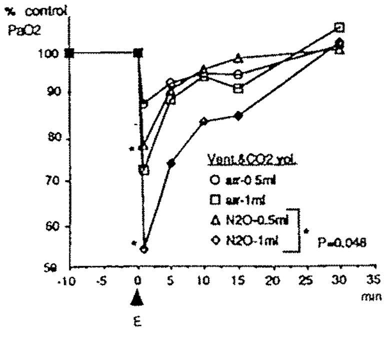
The baseline systolic-diastolic pattern of venous flow was replaced with PEEP by a predominant diastolic flow, the diastolic/systolic flow ratio increasing. This corresponded to a decreased systolic nadir (x descent) in Pra as the diastolic nadir (y descent) became prominent, similar to the pressure waveform observed with constrictive pericarditis but opposite to that seen with tamponade.
Discussion : With tamponade external constraint is uniform and coupled to total atrio-ventricular volume so that venous return is mainly during ventricular systole. During PEEP, the inflated lungs may add an external constraint which varies independently over the atrium and ventricle with the changes in the local chamber's volume. With added external constraint to the atrial and ventricular time varying elastances, the ratio of the systolic/diastolic effective elastances will be reduced more for the RA than the RV: i.e. the difference in pressures between contraction and relaxation of the atria becomes small, while the difference between ventricular systolic and diastolic pressures are still substantial. Thus, atrial relaxation has a diminished effect in increasing the gradient for systolic venous inflow (decreased x descent) but venous inflow will increase when the ventricle relaxes, i.e. with the y descent during diastole.
Conclusion: The Pra waveform and decrease in systolic venous inflow with PEEP resembles the independent pericardial constraint with constrictive pericarditis not the uniform constraint of tamponade.

A.90

TITLE : VENOUS CARBON DIOXIDE EMBOLI DOES NITROUS OXIDE MAKE DIFFERENCE?

AUTHORS : J.B. Nyarwaya MD*; S. Pierre MD**, V. Umbrain MD**; K.Samii MD*; A. d'Hollander MD,PhD**
AFFILIATIONS : *Dépt d'Anesth.-Réan, CHU Bicêtre, 94275 Le Kremlin-Bicêtre,France. **Dept of Anaesth, Erasmus Univ. Hospital, B-1070 Brussels, Belgium.

INTRODUCTION: It has been suggested that venous air emboli enlarge during ventilation with soluble and diffusible gas and thereby cause further vascular obstruction(1).The aim of this experimental study was to assess the differences in the pulmonay gas exchange impairments observed during ventilation with N_2O/O_2 as compared to air/O_2 mixture.
METHODS: After institutional approval, 12 piglets (weighing 24-27 kg) were located within two groups : N_2 group (n = 6) and N_2O group (n = 6) according to gas supplemented to O_2 (FiO_2: 0.30-0.35) for mechanical ventilation. Piglets were intramuscularly premedicated with azaperone and anaesthetized with a combination of ketamine and midazolam. Subsequent to tracheal intubation, allowed by intravenous pancuronium, and maintenance of surgical anaesthetic level with propofol, fentanyl and pancuronium, animals were instrumented for invasive monitoring and right intraventricular CO_2-embolisation. End-tidal partial pressure of CO_2($P_{ET}CO_2$), airway pressure (P_{aw}), lung compliance (C_L) and pulse oximetry (SpO_2) were continuously monitored using a Capnomac Ultima SV (Datex*, Helsinki, Finland). Haemodynamic variables including systemic arterial pressure (SAP), pulmonary arterial pressure (PAP), cardiac output, (Q_c), heart rate (HR) and electrocardiogram (ECG) were monitored. An 2-MHz ultrasonic probe (Sonicaid* Model D206, Chichester, England) was affixed on the precordium. After a stabilisation period, baseline values were recorded and CO_2-embolisation was performed in a crossover manner with 0.5 and 1 ml.kg^{-1} via a right intraventricular catheter. Studied variables were recorded as soon as embolisation completed and at 5, 10, 15 and 30 min. An analysis of variance (ANOVA) for repetitive measurements was used.
RESULTS : Four pools of data was obtained according to gas supplemented to O_2 and the volume of CO_2-bolus. Ultrasonic and $P_{ET}CO_2$ changes were noticed within 5 sec following the embolisation in all instances. Studied variables showed significant postembolic changes as compared to baseline values, except mean SAP, C_L and P_{aw}. A postembolic decrease was observed in PaO_2, $P_{ET}CO_2$, SpO_2, Qc values. The PAPm did not show significant differences between groups. Significant greater decreases in $P_{ET}CO_2$ (p=0.012) and PaO_2 (p=0.048; figure) were found in N_2O-group.
CONCLUSION : This study suggests that breathing N_2O may intensify pulmonary gas exchange impairments subsequent to venous CO_2-embolism. A marked shift of ventilation to higher V_A/Q regions and a shift of perfusion to low V_A/Q regions leading to serious alterations in O_2 and CO_2 exchange capabilities of the lung may result from N_2O flowing into the CO_2-bubbles . Therefore, a cautious use or avoidance of N_2O should be considered during extensive laparoscopic surgery.



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A.91

EFFECTS OF HYPOTHERMIA AND CAPTOPRIL ON ARTERIAL CONTRACTION

Eric Le Pelley*, Francois Le Brun*, Thierry Chataigneau**, Jean-Pierre Richer***, Robert Tricoche**, Jacques Fusciardi*

(*)Department of anaesthesiology and intensive care, (**)Laboratory of animal physiology, (***)GRTMV, University of Poitiers, Poitiers, France.

Background and goal of study : Captopril, an angiotensin-converting enzyme inhibitor, has a vasodilatory activity which depends on the renin-angiotensin system. It has also a direct endothelium-dependent vasodilatating action. During the induction of anaesthesia in patients treated by Captopril, hypotension is often observed. Usually, this hypotension can be prevented by blood volume expansion and successfully treated by vasopressor substances. However severe persistent hypotensions have been reported when hypothermia or hypovolemia is associated. The aim of this study was to investigate the effects of Captopril and/or hypothermia on the vascular response to vasopressor substances in swine femoral artery rings.

Materials and methods : Vascular rings (2.5 mm in length and 2 mm in diameter) were suspended in tissue baths at 37°C. and optimal tension determined. The integrity of the endothelium of each ring was assessed by the Acetylcholine (10^{-7} M)-induced reversion of KCl (20mM)-increased contraction. Then the rings were repeatedly washed, and the tension returned to the initial level. Renin (1mUI/ml) was added in all baths, and after 45 min. either Captopril (100μM) or water (control) were added. After 15 min., the rings were constricted with increasing doses (10^{-10} to 10^{-3} M) of Adrenaline (Ad), Noradrenaline (Nad), Phenylephrine (Phe), Ephedrine (Eph) Dopamine (Dopa) or Angiotensin II (AII). The same experiments were repeated with tissue baths at 30°C, to study the effect of hypothermia.

Results and discussion : At 37°C. the concentration-response curves for each vasopressor substance were the same with or without Captopril. Hypothermia alone shifted to the right the concentration response curves of Ad. Nad. Eph. Dopa. Captopril associated to hypothermia shifted to the right the concentration response curve of Phe but not the response of AII. This study shows that in hypothermia and presence of Captopril. the angiotensin II is the only one drug able to keep an intact arterial vasoconstrictive action. This result agrees with the conclusion of a case report (1).

Conclusion : These data further support the suggestion that (i) hypotension with Captopril permeation can react to sympathomimetic amines; (ii) in case of hypotension in hypothermia context without Captopril, phenylephrine is the only one sympathomimetic amine to keep an intact action power; (iii) in case of severe persistent hypotension in a context associating hypothermia and Captopril permeation, Angiotensin II is a first aid of these predicaments.

Reference : (1) THAKER U., GEARY K., CHALMERS P., et al.. J. cardiothorac. Anesth. 3: 360-363. 1990.

A.92

LONG-LASTING LAPAROSCOPY: INFLUENCE OF ANAESTHESIA ON HEMODYNAMICS IN PIGS.

O. Mansoor, J E Bazin, D. Pezet, P. Walleck, C. Monteillard.

Département d'anesthésie Centre hospitalier universitaire
63003 Clermont-Ferrand. France

Background and goal of study: The extend use of laparoscopy to complex procedures increases the duration of exposure to high intra-abdominal pressure. The aim of the present study was to compare the hemodynamic and the hepatic variations associated with a long CO_2-pneumoperitoneum (4 hours) with two anesthetic drugs which have different hemodynamic effects.

Materials and methods : Twelve "large white" pigs (mean weight 23.8 ± 4.5 kg) were anesthetized with intramuscular ketamine (10 mg/kg) and midazolam (0.3 mg.kg^{-1}). After oral intubation anAesthesia was maintained with nitrous oxide (50 % in oxygen) and ventilation was controled (Cicero-Dräeger). The end tidal pCO_2 ($PETCO_2$) and the concentration of isoflurane were continuously monitored (PM 8010 Dräeger). Ventilation was adjusted to keep $PETCO_2$ between 30-35 mmHg. The right external jugular vein and the right carotid artery were exposed to allow insertion of an arterial line and a 5.5 F thermodilution Swan-Ganz catheter (Opticath Abott). Immediately after (T0), the hemodynamic parameters : heart rate (HR), blood pressure (BP), right atrial pressure (RAP), pulmonary arterial pressure (PAP), cardiac output (CO) and systemic vascular resistance (SVR) were recorded. at the same time, a bolus of 0.5 mg/kgof indocyanine green (IG) was injected in order to defined hepatic blood flow (blood samples were taken at 2, 4, 8, 16 minutes after the injection to measure plasmatic concentrations by spectrophotometry). Then, either isoflurane was administred (1.5 vol%) in six randomly chosen pigs (Group I), or alfentanil (1ug.kg.min) in the six others (group A). Thirty minutes later, hemodynamic paremeters were recorded and an other bolus of IG was injected (T1). After that, a 15 mmHg CO_2-pneumoperitoneum was performed and maintened during 4 hours. Hemodynamic parameters and hepatic blood flow (HBF) were defined every hour (T2, T3, T4, T5) and 30 minutes after exsuflation of the pneumoperitoneum (T6). Results were expressed as mean ± SD. A Mann and Witney U-test was used to evaluate the relationships between the parameters of the two groups and in a same group an ANOVA analysis of variance was used ; a $p < 0.05$ was considered significant.

Results : They are presented in table 1.

	T0	T1	T2	T3	T4	T5	T6
MAP I	71.8 ± 23.2	51.7± 11.5	54.7 ± 12.2	58.0± 13.1	57.8 ± 17.7	61.0± 21.2	53.3 ± 19.1
MAP A	90.3 ± 15.5	91.5± 10.8	100.2± 15.9	106.8 ± 14.5	100.7± 28.3	104.7 ± 30.1	102.2± 32.2
CO I	3.2± 0.4	3.5± 1.6	3.2± 1.4	3.3± 1.1	2.8± 0.9	3.1± 1.3	3.1± 1.3
CO A	3.4± 0.9	3.4± 1.6	3.5± 1.6	3.7± 1.8	2.2± 0.8 ★	2.7± 1.9	3.1± 1.7
SVR I	1762 ± 802	1506 ± 578 ★	1565 ± 579	1520 ± 595	1643 ± 624	1509 ± 513	1548 ± 509
SVR A	2109 ± 671	2648 ± 1092 ☆	2586 ± 1299 ☆	2818 ± 1364 ☆	3778 ± 1637 ★ ☆	3631 ± 1719 ★ ☆	2887 ± 1345 ☆
HBF I	260± 101	202± 69	173± 63 ★	219± 83	178± 87	175± 97	212± 103
HBF A	227± 75	210± 72	188± 66	187± 65	201± 104	213± 120	231± 124

TABLE 1: MAP in mmHg, CO in l/min., svr in Dyn/s/cm^5 and HBF in ml/min.
☆$p < 0.05$ between the two groups ★$p < 0.05$ in the same group vs T0

Discussion and conclusion : The only significant difference between the two groups was the SVR variations and in consequence the increase of MAP in the group A. The HBF seemed less decreased, but not significantly in the group A.

A.93

HASTENING OF ISCHEMIA-INDUCED FALL OF ELECTRICAL FIBRILLATION THRESHOLD BY BUPIVACAINE AT MODERATE PLASMA LEVELS.

M. Freysz, M.D., Ph. D., L. Bertrix, M.D., Ph. D., J. Loufoua, Ph. D., Q. Timour, Ph. D., G. Faucon, M.D., Ph. D. Med. Pharmacol. Dept., Cl. Bernard University, Lyon, F - 69008, France.

Risk of ventricular arrhythmias and fibrillation is certainly increased in regional anesthesia with bupivacaine (B) by myocardial ischemia (I), since B largely shortens the time necessary to the triggering of fibrillation by a given experimental I (1). In order to approach the mechanism of this hastening of fibrillation occurrence, the electrical fibrillation threshold (EFT) was measured in anesthetized open-chest pigs, at the end of I of increasing duration, 30, 60, 120 and 180 s, obtained by temporary total occlusion of the anterior descending coronary artery near its origin. Measurement was performed with impulses of 100 ms duration at the rate of 180 bpm. Results were compared in the same animals in the absence and presence of B, i.v. administered in a loading dose of 1 mg/kg and an 25 min infusion of 0.04 mg/kg/min (plasma B levels between 1.4 and 1.8 µg/ml). Although B significantly raised EFT before coronary occlusion, the decline of EFT produced by I was faster in its presence, this hastening leading to an earlier spontaneous fibrillation which occurs when EFT falls down to the pacing threshold (about 0.30 mA). Therefore, the proportion of animals which fibrillated spontaneously after 60, 120 and 180 s I was higher when B was added. Concurrently, conduction time in the contractile ventricular fibers was lengthened, from 41 ± 4 to 79 ± 10 ms by B alone and up to 99 ± 8 ms under the combined influence of B and I. Asynchrony in the response of the fibers secondary to conduction disorders and, thereby, to sodium blocking properties of B is responsible for a defect in excitation which aggravates diastolic depolarization dependent on the metabolic blockade by I.

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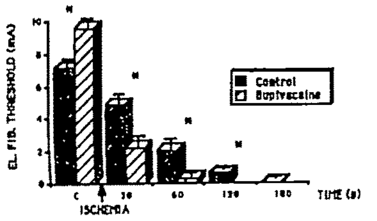


A.94

Is the difference between systemic and intramucosal pH – pH gap – an indicator of tissue ischaemia ?

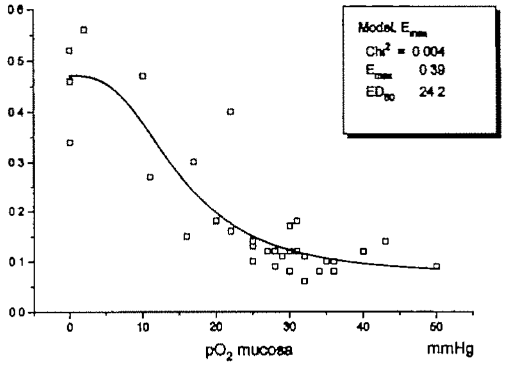
Sven Staender, Wolfgang Studer, Hans Pargger,
Olaf Schellscheidt, Karel Skarvan
Department of Anaesthesia, Kantonsspital, University of
Basel, 4031 Basel, Switzerland

Background and goal of study: Gastric tonometry (pH_i) has been recommended to detect imbalances between splanchnic mucosal oxygen supply and demand (1). To verify the relations between pH_i and mucosal oxygenation we measured polarographic mucosal surface pO_2 (ptO_2), determined pH_i, and calculated pH gap (systemic/intramucosal pH difference) as well as lactate production in a pig model of graded mesenteric ischemia.

Material and methods: 20 anaesthetised pigs had an electromagnetic flow probe and a screw occluder positioned around the superior mesenteric artery (SMA). Catheters were placed in the superior mesenteric vein, pulmonary artery, aorta, right atrium, a polarographic surface pO_2 electrode on the mucosa of and a tonometer inside the proximal ileum. Lactate was measured enzymatically and intestinal production calculated from the arterial/venous difference.

At the end of the surgical preparation, at least 60 minutes were allowed before baseline readings. SMA-blood flow was reduced to 100% (n=3, control), 50% (n=4), 37.5% (n=5), 25% (n=4) and 0% (n=4) of baseline flow. After 60 minutes flow reduction in each group, the second series of readings were obtained.

Results: With decreasing blood flow and development of intestinal lactate production we found a significant inverse, non-linear correlation between pH gap and ptO_2 (fig.) and a positive, non-linear correlation between pH_i and mucosal ptO_2 (sigmoidal E_{max}-model).



Conclusion: Both pH gap and pH_i reflect an oxygen supply/demand imbalance in the small intestine and may serve as an early indicator of intestinal ischaemia.

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A.95

CARDIOPULMONARY BYPASS AND TISSUE O2 EXTRACTION IN DOGS: PULSATILE Vs NON PULSATILE FLOW.

P. Van der Linden M.D.,Ph.D., G. Sahar M.D., M. Blauwaert Ph.D., Y.Bekkrar M.D., J-L. Vincent M.D., Ph.D.
Dpt Anaesthesiology, CUB Erasme, Brussels, Belgium.

Introduction. The effects of pulsatile Vs non pulsatile cardiopulmonary bypass (CPB) on tissue O2 extraction capabilities were compared in dogs during normothermia.

Material and methods. Eighteen mongrel dogs (28.3±3.6 kg) were anaesthetised with thiopental (20 mg/kg), fentanyl (bolus 50 mcg/kg + infusion 50 mcg/kg.h during the first hour and 25 mcg/kg.h thereafter) and pancuronium (0.1 mg/kg and 2 mg/h)) and mechanically ventilated with air. After sternotomy, an aortic and a right atrial cannula were inserted. Heparin was administered intravenously (± 5 mg/kg) to obtain a ACT above 500 sec. The bypass was then started, the aorta clamped, the heart arrested using 200 ml of standard cardioplegic solution and the lungs deflated. The dogs were perfused either with a continuous flow of 100 ml/kg/min (C group, N=9), or with the same flow given at a pulsatile rate of 80 movements/min (P group, N=9) (Stöckert Instrumente GmbH, München, Germany). The priming of the bypass included H.E.S. 450/0.7 6% and dog's red packed cells to obtain a haemoglobin concentration during CPB around 9 g/dl. During CPB, the dog's temperature was maintained at 37°C. Gas flow and FiO2 were adapted throughout the experiment to obtain a PaCO2 around 35 mmHg and a PaO2 above 150 mmHg. Mixed venous O2 saturation (SvO2) was continuously recorded. When the heart was arrested, a 30 min period was allowed to achieve steady-state, defined by a stable mean arterial pressure (MAP) and SvO2. The flow of the bypass was then progressively reduced by 10 ml/kg/min aliquots until 25 ml/kg/min. At each step, after a 10 min period to achieve a new steady state, MAP, pump flow, arterial and mixed blood gases and serum lactate were measured. O2 delivery (DO2) and O2 consumption (VO2) were calculated from standard formulas. In each dog, critical DO2 was determined from a plot of VO2 Vs DO2 (DO2crit) and from a plot of lactate Vs DO2 (DO2critLac), using a least sum of squares technique (1). O2 extraction at DO2crit (O2ERcrit) was obtained by dividing VO2crit by DO2crit. Groups were compared using a Mann Whitney U-test.

Results.	C group	P group	U-test
MAP (mmHg)	58 ± 16	52 ± 22	p=0.33
Flow (ml/min.kg)	57 ± 8.7	59 ± 13	p=0.78
VO2crit (ml/min.kg)	4.7 ± 0.7	3.9 ± 0.8	p=0.07
DO2crit (ml/min.kg)	7.7 ± 1.1	6.9 ± 1.8	p=0.20
DO2critLac (ml/min.kg)	7.8 ± 1.6	7.8 ± 2.3	p=0.90
O2ERcrit (%)	61 ± 7	57 ± 9	p=0.27

Conclusion. In the conditions of our study, O2ERcrit was similar in both groups. Therefore, our study does not support a beneficial effect of pulsatile bypass on tissue O2 extraction capabilities during normothermia.

Reference. (1) J Appl Physiol 64(5): 2074-2082, 1988.

A.96

INSPIRATORY MUSCLES STRENGTH AFTER INTERPLEURAL BUPIVACAINE IN HEALTHY HUMANS

Gallart L, Gea J*, Aguar MC*, Samsó E, Puig MM.

Departments of Anaesthesiology and *Pneumology.
Hospital Universitari del Mar and IMIM, Barcelona, Spain.

BACKGROUND & GOAL OF STUDY

The effects of Interpleural Anaesthesia (IPA) on diaphragmatic function remain controversial. Electromyographic activity of this muscle appears to decrease in a canine model (1), but no research has been carried out to assess the effects of IPA on inspiratory muscle pressures. The aim of this study was to evaluate these in healthy subjects.

PATIENTS & METHODS

Ten patients, with I-II ASA physical status and normal respiratory function tests, scheduled for cholecystectomy, entered the study.

Inspiratory muscles strength was assessed by measuring transdiaphragmatic (PDI) and mouth (MIP) maximal inspiratory pressures. PDI was obtained with the two balloon-catheter technique, and was calculated from the difference between oesophageal (Pes) and gastric (Pga) pressures. MIP was measured during an occlusion manoeuvre from residual volume.

Functional reserve against fatigue was estimated through the tension-time index for the diaphragm (TTDi = $\overline{PDI}$/PDImax X Ti/Ttot; where $\overline{PDI}$ is PDI at Tidal Volume; PDI max, maximal PDI obtained with a sniff manoeuvre; Ti, inspiratory time; and Ttot, total respiratory time).

Muscles strength and reserve, breathing pattern (BP), forced spirometry (FS) and static lung volumes (LV) were evaluated in supine position before and after the administration of IPA (bupivacaine 0,5% 20 mL with epinephrine 1/200.000). Arterial pressure (AP), heart rate (HR) and SaO_2 were monitored throughout the study. Data are expressed as mean and standard deviation, and paired t-tests were used to detect changes.

RESULTS & DISCUSSION

After IPA, no significant changes were found in values from BP, FS, LV, AP, HR and SaO_2. Regarding to respiratory pressures and related parameters, $\overline{PDI}$, maximal Pes (Pesmax) $\overline{PDI}$/PDImax, TTDI and MIP remained unchanged. By contrast, there was a slight but significant decrease in PDImax.

	Pesmax (cm H_2O)	PDImax (cm H_2O)	TTDI	MIP (% ref.)
Pre-IPA	-78±19	95±11	0.02±0.007	117±28
Post-IPA	-75±17	86±12	0.02±0.009	106±35
p value	NS	<0.05	NS	NS

The change in PDImax suggests a slight decrease in diaphragm maximal strength after IPA. However, it has probably little clinical relevance considering the small value of the decline, and that TTDI, MIP, Pesmax , and FS values remained unchanged.

CONCLUSION

IPA, when administered as described in healthy humans, slightly decreases maximal transdiaphragmatic pressure without modifying other respiratory muscle strength and lung function tests.

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A.97

DIAPHRAGMATIC FUNCTION AFTER BUPIVACAINE (B) VS LIDOCAINE (L) CERVICAL EXTRADURAL ANALGESIA FOR CHRONIC PAIN THERAPY

Elisabet Nyström, Erika Jansson, Britt-Inger Wenngren, Francois Clergue, Sebastian Reiz.

From the Departments of Anaesthesia and Otorhinolaryngology, University of Umeå, Umeå, Sweden and the Department of Anaesthesia, Tenon University Hospital, Paris, France

Background & goal of study: A discrete impairment of respiratory function by cervical ED with B, possibly related to CNS absorption of this lipophilic drug has previously been documented (1). This study examines the effects of L versus B administered randomly in equianalgesic doses into the cervical extradural region on diaphragmatic function, arterial blood gases and occulomotor function.

Patients & methods: 14 ambulatory patients with chronic pain due to osteoarthrosis were studied. Four patients participated twice. They all had an ED catheter inserted to the C5 level via the C7/T1 interspace through which 15 mg of B (3 ml) (n=9) or 60 mg of L (3 ml) (n=9) mixed with 1 ml (40 mg) of depomedrone were injected after baseline measurements. These consisted of gastric (Pga) and oesophageal pressures (Poes), transdiaphragmatic pressure (Pdi), the relative contribution of rib cage and abdomen to quiet tidal breathing (Respitrace®), blood gases and oxygen saturation. In addition, we assessed occulomotor function (2). All measurements were repeated 30 min after ED.

Results: L and B produced blocks from C3±1 to T5±1 and from C3±1 to T6±1 respectively. Pdi and Pga/Pdi were not affected by L or B. Other results are presented in the table.

Table: Heart rate (HR), blood gases, Respitrace® data and occulomoteor function (i.e. velocity of volontary saccadic eye movement, VVSEM).

	Lidocaine		*Bupivacaine*	
	control	*ED*	*control*	*ED*
HR (bpm)	81±7	73±10[a]	74±13	69±11
paCO2 (kPa)	5.4±0.4	5.5±0.5	5.3±0.3	5.5±0.5
paO2 (kPa)	10.4±1.3	9.8±1.6	10.4±1.4	9.8±1.1[b]
SpO2 (%)	95±2	95±2	97±2	95±3
VT (ml)	443±184	465±212	437±90	380±67
***volth/abd* (%)**	28/72	27/73	26/74	25/75
VVSEM (°/sec)	362±44	352±39	393±46	369±53[c]

a: p=0.001, b: p=0.044, c: p=0.005

Discussion and conclusions: Neither drug affected diaphragmatic function or altered abdominal/rib cage contribution to quiet tidal breathing. In contrast to L, B decreased occulomotor function and produced marginal decrease in arterial oxygen tension. The results after B concur with previous data (1). It is suggested that L does not diffuse to occulomotor nuclei as effectively as B and thereby might affect adjacent respiratory nuclei to a lesser degree than B.

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A.98

Relaxant Action of Ketamine Isomers on Isolated Porcine Tracheal Muscle.

K. Rehder, A. Ebberyd, C. Ingrassia, C. Wiklund, S.G.E. Lindahl, Department of Anaesthesiology, Karolinska Hospital, S-171 76 Stockholm, Sweden

Background and Goal of the Study:
Ketamine (K) is used clinically as a racemate (R.K.), consisting of equal parts of the dextro- (D.K.) and levorotatory (L.K.) isomers. The R.K. is a potent bronchodilator both in vivo (1) and in vitro (2), but the effect of the isomers on the airways is not known. It was the purpose of this study to compare their effects on isolated porcine tracheal muscles.

Materials and Methods.
Strips of porcine tracheal muscle (without epithelium) were suspended in organ baths filled with physiological salt solution (37°) bubbled with 95% O_2 and 5% CO_2. Isometric forces of the muscles were recorded at the optimal length, and the maximal force (response to 10^{-4} M acetylcholine; ACh) was determined. Cumulative concentration-response curves to ACh (10^{-9} to 10^{-4} M, half-log increments) were obtained in muscles from 6 pigs after the muscles had been incubated with 10^{-6} M Tetrodotoxin (TTX). In muscles from 5 other pigs non-cumulative concentration-response curves to 1,1 - dimethyl - 4 phenylpiperazinium iodide (10^{-6} to 10^{-4} M; DMPP) were obtained. All studies were performed first in the absence and then after incubation with 10^{-5} or 10^{-4} M R.K. or L.K., or D.K. The effects of K on the concentration response curves were analyzed by repeated measures analysis of variance.

Results and Discussion:
10^{-5}M of K or its isomers had no significant effect on the concentration-response curves to ACh or DMPP. By contrast, 10^{-4}M of R.K., L.K. and D.K. abolished the excitability of the postsynaptic nicotinic receptors in the intramural ganglia, indicating a prejunctional or "indirect" effect. 10^{-4} M of R.K., L.K. and D.K. also shifted the concentration-response curves to ACh to the right. This indicates a postjunctional or "direct" effect, since it occurred in the presence of 10^{-6}M TTX. The effect of L.K. was more pronounced than that of R.K. Although comparisons between in vitro and in vivo studies and between various species are of limited value, the results of the studies suggest that the bronchodilating effect of L.K. and R.K. should be compared in humans.

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A.99

OPIOID RECEPTORS IN ISOLATED BOVINE TRACHEAL MUSCLE.

L.Zappi, K.Rehder, D.Rocchi, V.Brusasco, F.Nicosia, Department of Anaesthesiology, National Institute for Cancer Research, Genova, Italy.

Background and Goal of the Study:
Opioid agonists attenuate cholinergic neurotransmission in guinea pig (1), canine (2) and human airways (3). In the laryngeal part of the trachea of the guinea pig no such inhibitory effect could be demonstrated (1). We wondered if an inhibitory effect existed in the bovine trachea and if it was present only in the carinal part.

Materials and Methods:
Strips of bovine tracheal muscles were suspended in organ baths filled with physiological salt solution (37°C) bubbled with 95% O_2 and 5% CO_2 (epithelium removed).Isometric force at optimal length was recorded. Eight strips of trachealis muscle were examined from 6 animals. Two samples, each taken from the upper, upper middle, lower middle or lower part of the trachea. All strips were incubated with 10^{-6}M of propanolol and 10^{-5}M of indomethacine.The frequence-response curves to electric field stimulation (EFS)(0.5 ms, 15V, 0.1 to 32 Hz) were recorded. Thereafter, one muscle strip from each of the 4 sections of the trachea was incubated with 10^{-5}M of the μ-opioid agonist DAMGO 4D-Ala^2;$NMePhe^4$,$Glyol^5$,enkephalin), and the EFS was repeated. The other 4 muscles served as control for the effects of time.

Results and Discussion:
10^{-5}M of DAMGO inhibited the response to EFS at low stimulation frequencies (0.1 to 1 Hz). The response was similar in all 4 sections. These results suggest that μ-receptors attenuate cholinergic neurotransmission in the entire bovine trachea and the attenuation of the neurotransmission is not due to increased release of catecholamines. This reduction in cholinergic neurotransmission in airways may have therapeutic value for the treatment of bronchospasm during anaesthesia.

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A.100

IN-VITRO RESISTANCE OF DOUBLE-LUMEN ENDOBRONCHIAL TUBES: EFFECTS OF TUBE SIZE AND SIDE

P. Debay, G Bardoczky, A. Van Muylem, JM. Moures,
A. d'Hollander

Department of Anesthesiology and Chest Medicine
Erasme University Hospital, Brussels, Belgium

INTRODUCTION: As there are no data about the resistance of the disposable PVC double-lumen endobronchial tubes (DLT), we performed an in-vitro study to document the flow resistance according to the size and the type (left or right sided) of the DLTs with increasing inspiratory flow rate.

MATERIALS AND METHODS: Four available size (35F, 37F, 39F and 41F) of the DLT (Broncho-Cath, Mallinckrodt, England) employed in our institution were studied; for each size both the left and right sided version were tested. Three airflows (4.5, 9.0 and 13.5 L/min) were administered by the Siemens 900C ventilator the common connector of the DLT. Flow was measured with a Lilly type pneumotachograph connected to a differential pressure transducer. The pressure and flow signals were electronically processed to give a measurement of resistance. The signal was delivered and displayed on an Olivetti microcomputer via a twelve bits analog-to -digital converter (rate of conversion 50Hz). Data were compared by the Student t-test, $P < 0.001$ considered as significant.

RESULTS: The main results of the study are summarized in table 1

	Flow 4.5L/min	Flow 9 0L/min	Flow 13.5L/mm	
35 L-left lumen	7.99 (0 09)	13.34 (0.16)	22.82 (0.16)	0.0001
37 L-left lumen	7.41 (0.15)	12.34 (0.14)	20.94 (0.36)	0.0001
39 L-left lumen	6.65 (0.08)	11.30 (0.19)	18.07 (0.16)	0.0001
41 L-left lumen	6.53 (0.08)	12.39 (0.19)	17.74 (0.21)	0.0001
35 R-right lumen	7.79 (0.07)	13.95 (0.21)	21.93 (0.25)	0.0001
37 R-right lumen	7.15 (0.06)	13.61 (0.13)	20.26 (0.34)	0.0001
39 R-right lumen	6.42 (0.07)	12.08 (0.15)	17.98 (0.20)	0.0001
41 R-right lumen	6.10 (0.04)	11 49 (0.17)	17.18 (0.19)	0.0001

DISCUSSION and CONCLUSIONS: The in-vitro resistance of the DLTs increased significantly with increasing the flow rate, and as their internal diameter decreased. For the same size, there were no difference in resistance between the left and right sided DLTs. Based on its resistances, the DLTs can be divided in two groups: the 35F and 37 F (small) group with higher resistance,and the 39F and 41 F (large) group with low resistance to airflow. Since there is a large step-up of resistance between the 37F and 39F sizes, where there is possible, the larger DLT with a lower resistance should be chosen.

A.101

TITLE: EFFECTS OF EXTERNAL PEEP ON RESPIRATORY MECHANICS DURING ONE LUNG VENTILATION

Authors: G. Bardoczky MD, JC Yernault MD. PhD, JM. Moures MD, P. Rocmans MD.PhD.

Affiliation: Erasme University Hospital, Brussels, Belgium

INTRODUCTION: During one-lung ventilation(OLV), application of external PEEP (PEEPe) to the dependent lung has been suggested to improve oxygenation. The various results might be due to the additive effect between PEEPe and preexisting intrinsic PEEP (PEEPi)(1). PEEPi can be demonstrated and the impact of PEEPe can be evaluated immediately with on-line flow-volume (FV) curves.

METHODS: 6 consenting patients undergoing elective thoracotomy with OLV were studied after IRB approval. Patients were anesthetized, paralyzed, their trachea was intubated with a double-lumen endotracheal tube. Their lungs were ventilated with a Siemens 900C ventilator set to deliver a constant tidal volume (10 ml/kg) with a square wave flow profile, at a rate of 10-11 bpm. Inspiratory hold was 10% of the total cycle, T_E was 3s. Ventilatory data were recorded with the Ultima (Datex, Finland) on-line respiratory monitor. Measurements were obtained during OLV, at 0,2,4,6,8 and 10 cmH_2O PEEPe. Data were analyzed with Friedman's two way ANOVA, $P< 0.05$ was considered significant.

RESULTS & DISCUSSION: The main results are summarized in table 1. All the patients exhibited PEEPi during OLV evidenced by the FV curves. For the patients in this study, increasing PEEPe was not associated with substantial changes in the pressure-volume and flow characteristics of the total respiratory system, but with significantly increased inspiratory airway pressures. The slight increase of expiratory flow at +4 and +6 cmH_2O PEEP indicates that PEEPe exceeded the critical pressure for expiratory flow limitation.

CONCLUSIONS: On-line monitoring of ventilation and display of FV curves provides a simple way to assess the presence of dynamic hyperinflation and to monitor the effects of PEEPe on expiratory flow and helps to titrate PEEPe in small steps to avoid the administration of excessive external PEEP.

Table 1. Ventilatory data of 6 patients during OLV.
* $P < 0.05$

Ventilatory data	ZEEP	+2 PEEP	+4 PEEP	+6 PEEP	+8 PEEP	+10 PEEP
Vt_{insp} (ml)	671(61)	673(62)	673(60)	676(61)	660(61)	655(78)
Vt_{exp} (ml)	662(63)	666(71)	661(55)	661(70)	649(54)	639(72)
Ppeak (cmH2O)	21(6)	22(5)	25(6)	28(5) *	32(5) *	35(6) *
Pplateau (cmH2O)	13(3)	15(3)	17(3) *	20(2) *	23(2) *	25(3) *
C_{rs} (ml/cmH2O)	54(13)	53(14)	51(13)	49(7)	46(7)	46(7)
PEV %	48(7)	46(5)	50(5)	51(8)	47(7)	47(5)

Ref: 1. Slinger, Cardiothor & Vasc Anesth Update 1991:2:1-11.

A.102

INHALED NO REDUCES ALVEOLAR DEAD SPACE IN PATIENTS WITH ARDS AND PULMONARY HYPERTENSION

J. J. Rouby, L. Puybasset, E. Mourgeon, A. M. Descouls,
A. M. Korinek, P. Viars.
Surgical Critical Care Unit,
Department of Anesthesiology, La Pitié Hospital,
University of Paris VI, France.

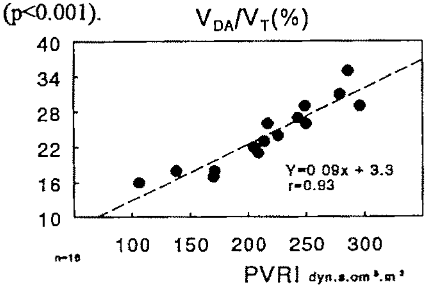
Inhaled NO has been shown to decrease pulmonary artery pressure and to improve arterial oxygenation in patients with ARDS and pulmonary arterial hypertension. The aim of this study was to assess the effects of inhaled NO on alveolar dead space (V_{DA}/V_T) and CO_2 elimination.

Patients and methods. In 7 patients (mean age 48 ± 24 yrs), mechanically ventilated (TV = 670 ± 203 ml, F = 19 ± 2/min, PEEP = 10 cm H_2O, FIO_2 100%) for an ARDS (lung injury severity score > 2.5), hemodynamic parameters obtained from a fiberoptic swan-ganz catheter, blood gases and end-expiratory CO_2 partial pressure ($PetCO_2$) obtained from an infrared capnometer, were measured before and after the administration of 2 ppm of inhaled NO. NO concentrations were measured within the endotracheal tube using a bedside chemiluminescence apparatus (NOX 2000, Séres, France). Pulmonary shunt (Q_s/Q_t), V_{DA}/V_T and pulmonary vascular resistance index (PVRI) were calculated using standard formula.

Results. Inhaled NO significantly decreased MPAP from 32 ± 5 mmHg to 28 ± 5 mmHg and PVRI from 418 ± 117 dyn.s.cm-5.m-2 to 370 ± 120 dyn.s.cm-5.m-2 ($p<0.001$). As shown in the table, inhaled NO significantly decreased $PaCO_2$, Q_s/Q_t and V_{DA}/V_T.

* $p<0.05$ NO vs control	PaO_2 mmHg	Q_s/Q_t %	$PaCO_2$ mmHg	$PetCO_2$ mmHg	V_{DA}/V_T %
Control	193±63	35±4	41±6	27±3	33±7
NO = 2 ppm	286±84*	29±5*	39±6*	27±4	29±10*

In one patient, PVRI and V_{DA}/V_T were measured 8 times with and without NO throughout a 45-day period. As shown in the figure, PVRI and V_{DA}/V_T were highly correlated ($p<0.001$).



Conclusion. These results suggest that, by reversing pulmonary arterial vasoconstriction, inhaled NO re-open pulmonary vessels in ventilated lung areas.

A.103

COMPARATIVE EFFECTS OF INHALED NO IN ZEEP AND PEEP CONDITIONS IN PATIENTS WITH ARDS

E. Mourgeon, L. Puybasset, J. J. Rouby, S. Dreux, P.
Poete, P. Viars.
Surgical Critical Care Unit,
Department of Anesthesiology, La Pitié Hospital,
University of Paris VI, France.

In patients with ARDS, inhaled NO partially reverses pulmonary arterial hypertension and improves arterial oxygenation. The aim of the present study was to assess whether these beneficial effects could be enhanced by the administration of PEEP.

Patients and methods. In 11 patients (mean age 51 ± 21 yrs), mechanically ventilated (TV 687 ± 180 ml, F 19± 2/min, FIO_2 100%) for an ARDS (lung injury severity score > 2.5), hemodynamic and respiratory parameters obtained from a fiberoptic swan-ganz catheter were measured in 4 different conditions : ZEEP, ZEEP NO, PEEP, PEEP NO. Inhaled NO was administered at a concentration of 2 ppm as measured within the endotracheal tube by a bedside chemiluminescence apparatus (NOX 2000, Séres, France). Pulmonary shunt (Q_s/Q_t) and pulmonary vascular resistance index (PVRI) were calculated using standard formulae.

Results. As shown in the table, the NO induced increase in PaO_2 was significantly greater in PEEP (45 ± 26%) conditions than in ZEEP (30 ± 20%) conditions, (p = 0.004). In contrast, the NO induced pulmonary arterial vasodilation was not significantly different in both conditions.

*$p<0.05$ NO vs control	PaO_2 mmHg	Q_s/Q_t %	MPAP mmHg	PVRI dyn.s.cm-5.m-2
ZEEP	141±74	41±11	29±8	395±186
ZEEP NO	179±85*	38±9*	26±1*	336±137*
PEEP	180±70	36±5	30±7	451±156
PEEP NO	254±92*	31±7*	27±5*	366±143*

These results suggest that pulmonary vascular effects of inhaled NO are independant of alveolar recruitment whereas the effects on arterial oxygenation are markedly alveolar recruitment dependent.

A.104

EFFECTS OF INHALED NITRIC OXIDE (NO) ON RESPIRATORY RESISTANCE IN PATIENTS WITH ARDS

E. MOURGEON MD, L. PUYBASSET MD, L. BODIN MD, J. J. ROUBY MD, PhD, P. VIARS MD,PhD
Surgical Critical Care Unit, Department of Anesthesiology, Hopital de la Pitié, University Paris VI, FRANCE

Respiratory resistance is abnormally elevated in patients with ARDS and could contribute to VA/Q abnormalities and hypoxemia (1,2). It was recently demonstrated that inhaled NO improves arterial oxygenation in patients with ARDS (3) and is a potent bronchodilator in guinea pigs (4). The aim of this study was to measure the effects of inhaled NO on respiratory resistance in patients with ARDS. **METHODS:** Eleven patients (mean age 57±21 yrs) with ARDS were prospectively studied after informed consent and institutional approval were obtained. Under intermittent positive pressure ventilation, they had a mean PaO2 of 171±84 mmHg (FiO2 1, ZEEP), a mean pulmonary artery pressure of 29±9 mmHg, a mean pulmonary shunt of 36±6%, a mean VD/VT of 35±11% and a mean respiratory compliance of 55±18 ml/cm H2O (gross syringe method). All patients were paralyzed (vecuronium) and ventilated using a constant inspiratory flow. Airway pressure was obtained from an intratracheal catheter and gas flow was measured using a heated Hans Rudolph 3500 B pneumotachograph. Total inspiratory resistance (Rrs max) was measured using the end-inspiratory airway occlusion technique (5). Normal values using this technique have been reported to be 3-5 cm H2O/l/s2. NO, released from a tank of nitrogen with a NO concentration of 2235 ppm (Air Liquide, France), was continuously administrated within the inspiratory limb of the ventilator at flow rates which produced concentrations of 10, 20, 40 and 80 ppm within the trachea. Intratracheal concentrations of NO and NO2 were measured using 2 electrochemical cells for NO and NO2, previously calibrated and validated using chemiluminescence. Following each NO administration, control measurements were systematically performed. An analysis of variance for repeated measures was used to analyse the effect of increasing concentrations of NO on Rrs max. **RESULTS:** As shown in the table, NO had no effect on Rrs max (±sem) at any concentration.

ppm	C1	10	C2	20	C3	40	C4	80	C5
Rrs max	12,3 ±2,2	11,2 ±2,3	11,8 ±2,4	11,6 ±2,1	11,5 ±2,3	12,1 ±2,6	12,0 ±2,3	11,4 ±2,4	11,7 ±2,2

CONCLUSION: Inhaled NO has no bronchodilator effect in ARDS patients with elevated Rrs max. This result contrasts with an experimental study suggesting a potent bronchodilator effect (4). Consequently, it is unlikely that the NO induced beneficial effect on ventilation-perfusion ratios in ARDS patients, is related to a bronchodilation.

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5. Intensive Care Med 1988, 14, 547-553.

A.105

RESPIRATORY EFFECTS OF INHALED NITRIC OXIDE AT A CONCENTRATION OF 10-80 PPM.

L. PUYBASSET MD, E. MOURGEON MD, J. J. ROUBY MD, PhD,P. POETE MD, P. VIARS MD, PhD
Surgical Critical Care Unit, Department of Anesthesiology, Hopital de la Pitié, University Paris VI, FRANCE

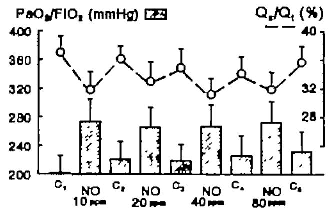
It has recently been demonstrated that inhaled nitric oxide (NO) decreases pulmonary artery pressure (MPAP) and pulmonary vascular resistance (PVR) and improves arterial oxygenation in patients with ARDS. Experimentally, inhaled NO has been shown to reverse the acute pulmonary vasoconstriction induced by the infusion of an endoperoxide analogue of thromboxane in a dose-dependent manner in the range 5-80 ppm (1). The aim of this study was to investigate whether respiratory effects of inhaled NO in patients with ARDS are dose-dependent in the range 10-80 ppm.

METHODS:

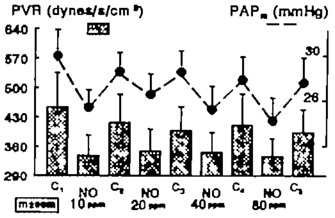
Nine patients (mean age 65±12 yrs) with ARDS were prospectively studied after informed consent and institutional approval had been obtained. NO, released from a tank of nitrogen with a NO concentration of 2235 ppm (Air Liquide, France) was continuously administered within the inspiratory limb of the ventilator at flow rates which produced NO concentrations of 10, 20, 40 and 80 ppm within the trachea. Intratracheal concentrations of NO and NO2 were measured using 2 electrochemical cells for NO and NO2, previously calibrated and validated using chemiluminescence. Between each NO concentration, control hemodynamic and respiratory measurements were systematically performed. An analysis of variance followed by a multiple comparison test was used to analyse the respiratory and hemodynamic effects of increasing concentrations of NO (data are mean ± sem).

RESULTS:

As shown in figure 1, inhaled NO induced a non dose-dependent increase in PaO2/FIO2 associated with a decrease in Qs/Qt . (p<0.01 and p<0.01,respectively).



As shown in figure 2, inhaled NO induced a non dose-dependent decrease in PVRI and MPAP (p< 0.01 and p < 0.01 respectively).



All other hemodynamic and respiratory parameters remained unchanged

CONCLUSION:

This study shows that the beneficial effects of inhaled NO on arterial oxygenation and pulmonary circulation observed in patients with ARDS are not dose-dependent in the range 10 to 80 ppm. 1. Frostell et al, Circulation 83: 2038-2047.

A.106

DOSE-RESPONSE OF NITRIC OXIDE INHALATION IN EARLY ACUTE LUNG INJURY.

Stefan Lundin, Ulla Westfelt, Ola Stenqvist, Hans Blomqvist, Annika Lindh, Lars Berggren, Claes G Frostell.
Depts of Anesthesia & Intensive Care, Sahlgren's Hospital, Göteborg, Danderyd Hospital, Danderyd, Huddinge Hospital, Stockholm & Örebro Hospital, Örebro, Sweden.

Background & goal of study: Previous dose-response studies have shown that nitric oxide inhalation may improve oxygenation and decrease an elevated pulmonary artery pressure in patients with severe lung injury (ARDS).[1] We have studied the effects of inhaled nitric oxide(NO) in 10 patients (ages 22-83 years) with moderate acute lung injury (ALI) of varied etiology.

Material & methods: Patients selected had a PaO_2/FiO_2 ratio of less than 20 kPa for more than 24 hrs but less than 72 hrs at PEEP ≥ 5 cm H_2O, Murray score being around 2. Prior to NO inhalation mean pulmonary artery pressure (MPAP) and pulmonary capillary wedge pressure (PCWP) were 30±2 and 13±1 mm Hg respectively, while cardiac output (CO) was 8.0±1.0 L/min. A nitric oxide inhalation system[2] was used to deliver NO (1000 ppm in N_2) and O_2/air to the fresh gas inlet of a Siemens 900C ventilator. NO and NO_2 concentration were measured by fuel-cell technique (City Technology, London, GB). Haemodynamics and pulmonary gas exchange were measured at baseline and at stepwise increased NO concentrations of 0.1, 0.3, 1, 3, 10, 30 and 100 ppm; each dose maintained for 15 min.

Results & Discussion: NO inhalation produced a significant (ANOVA; $p<0.01$) increase in PaO_2 being 8.4±0.3 kPa at baseline and 12.0±1.1 kPa at the optimal NO dose. This NO dose varied between individuals from 0.3 to 100 ppm, the median dose being 10 ppm. Mean Qs/Qt was reduced from 39±3 to 30±4%. There were no significant change in MPAP, PCWP or CO over this dose-range.

Conclusion: The study shows that NO inhalation improves oxygenation in patients with early ALI. Only small reductions in MPAP-PCWP was detected in some patients.

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2. Stenqvist O, Kjelltoft B, Lundin S. Acta Anest Scand 1993;37:687-691.

A.107

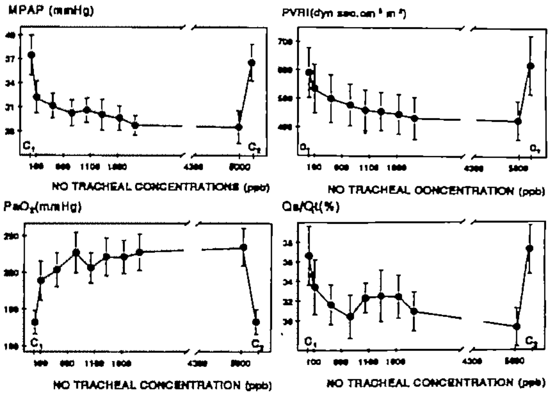
INHALED NO IN ARDS : DOSES-RESPONSE CURVES.

L. Puybasset, J. J. Rouby, E. Mourgeon, S. Dreux,
A. M. Korinek, P. Poete, P. Viars.
Surgical Critical Care Unit, Department of
Anesthesiology, La Pitié Hospital, University of Paris VI,
France

Inhaled nitric oxide (NO) vasodilates preconstricted human pulmonary arteries without causing systemic vasodilation. The aim of this study was to determine the dose-response curves of inhaled NO in terms of pulmonary vasodilation and improvement in PaO_2 in patients with ARDS.

Patients and methods. Six critically ill patients with severe acute respiratory failure (lung injury severity score > 2.5) and pulmonary hypertension, received 8 inhaled NO concentrations for a 15-min period in a random order : 100, 400, 700, 1000, 1300, 1600, 1900 and 5000 ppb. Hemodynamic parameters were measured using a fiberoptic swan-ganz catheter and continuously recorded on a Gould ES 1000 recorder. Blood gases, SaO_2, SvO_2, hemoglobin and methemoglobin blood concentrations were measured using an OSM_3 co-oximeter. NO and NO_2 concentrations were measured using a bedside chemiluminescence apparatus (NOX 2000, Séres, France, continuous aspiration -150 ml/min). Control measurements were made before (C_1), and after (C_2) the administration of inhaled NO.

Results. As shown in the figures, inhaled NO induced dose-dependent changes in PaO_2, Q_s/Q_t, pulmonary vascular resistance index (PVRI) and MPAP in the range 100-1900 ppb. No changes in heart rate, arterial pressure, cardiac output and systemic vascular resistance were observed.



Conclusion. This study suggests that therapeutic concentrations of inhaled NO in patients with ARDS are around 2 ppm and that the administration of greater concentrations is unnecessary.

A.108

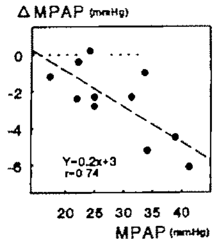
INHALED NO IN ARDS : PREDICTIVE FACTORS OF PULMONARY EFFECTS

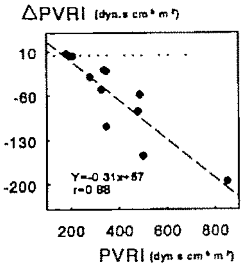
L. Puybasset, E. Mourgeon, J. J. Rouby, M. Samama,
M. Diaby, P. Viars.
Surgical Critical Care Unit,
Department of Anesthesiology, La Pitié Hospital,
University Paris VI, France

Inhaled NO decreases mean pulmonary arterial pressure (MPAP) and increases PaO_2 in some patients with ARDS and acute pulmonary hypertension (responders) and has no effect in others (non-responders). The aim of this study was to determine if the initial values of MPAP, pulmonary vascular resistance index (PVRI), PaO_2 pulmonary shunt (Q_s/Q_t) and static respiratory compliance measured using the gross syringe method (Crs) measured in ZEEP conditions and at FIO_2 1, were predictive of the effects of inhaled NO on the pulmonary circulation and on arterial oxygenation.

Methods : eleven patients (mean age 54 ±21 yrs) with ARDS (lung injury severity score > 2.5) and arterial pulmonary hypertension were prospectively studied after informed consent and institutional approval had been obtained. Hemodynamic and respiratory parameters, obtained from fiberoptic Swan-Ganz and arterial catheters were measured in ZEEP conditions (FIO_2 1) without NO and following the administration of 2 ppm of NO. NO concentrations were measured within the endotracheal tube using a bedside chemiluminescence apparatus (NOX 2000, Sérès, France). With NO, changes in MPAP, PVRI, PaO_2 and Q_s/Q_t were correlated with MPAP, PVRI, PaO_2, Q_s/Q_t and Crs measured in ZEEP conditions without NO, using a linear regression analysis (20 correlations were tested).

Results : No correlations were found between the initial values of PaO_2 , Q_s/Q_t and Crs and inhaled NO induced changes in MPAP, PVRI, PaO_2 and Q_s/Q_t. As shown in the figures, only 2 statistically significant correlations were found between the decrease in MPAP and the control values of MPAP (r = 0.74, p = 0.001) and between the decrease in PVRI and the control values of PVRI (r = 0.88, p = 0.001).





This study demonstrates that the greater the initial PVRI and MPAP, the greater the NO induced decrease in PVRI and MPAP. In ZEEP conditions, the effect of inhaled NO on pulmonary oxygenation is independant of the initial values of MPAP, PVRI, PaO_2 , Q_s/Q_t and Crs.

A.109

REVERSAL OF HYPERCAPNIA INDUCED ACUTE PULMONARY HYPERTENSION BY INHALED NITRIC OXIDE (NO)

L. PUYBASSET MD, T STEWART MD, E. MOURGEON MD, J. J. ROUBY MD, PhD, M DIABY MD, P. VIARS MD, PhD Surgical Critical Care Unit, Department of Anesthesiology, Hopital Pitié-Salpêtrière, University of Paris VI, FRANCE

In severe ARDS, hyperventilation of healthy regions of the lung might exacerbate alveolar injury via pulmonary barotrauma. Permissive hypercapnia has been recently advocated as a method of prevention. A rapid increase in PaCO2 generally induces an acute pulmonary hypertension which could be deleterious in patients with ARDS by increasing microvascular filtration pressure and pulmonary edema. The aim of this study was to assess whether inhaled NO could reverse hypercapnia induced pulmonary hypertension in patients with ARDS. **METHODS**: Nine patients (mean age 55±23 yrs) with ARDS were prospectively studied after informed consent and institutional approval were obtained. All patients were deeply sedated and had a Swan-Ganz catheter for purpose of cardiovascular monitoring. Each patient was initially ventilated using a VT of 8 ml/kg, a PEEP of 10 cm H2O and a FiO2 of 100%. Permissive hypercapnia was then induced by reducing VT to 4 ml/kg. NO, released from a tank of nitrogen with a NO concentration of 2235 ppm (Air Liquide, France) was continuously administered within the inspiratory limb of the ventilator at a flow rate which produced an intratracheal concentration of 2 ppm. Intratracheal concentrations of NO and NO2 were measured using chemiluminescence (NOX 2000, Serès, France). NO was administered in both normocapnic and hypercapnic conditions. **RESULTS:** Acute hypercapnia induced a major increase in mean pulmonary arterial pressure (MPAP), due to an increase in cardiac output and in pulmonary vascular resistance index (PVRI), associated to a marked rise in blood norepinephrine (NE) concentration. Despite an increase in Qs/Qt, PaO2 remained unchanged due to the increase in SvO2. Inhaled NO at a concentration of 2 ppm totally reversed the increase in PVRI induced by acute hypercapnia, without changing CI.Inhaled NO reduced PVRI by 23±13% in hypercapnic conditions vs 11±6% in normocapnic conditions (p<0.05).

mean±sd	**NC**	**NC+NO**	**HC**	**HC+NO**
pCO2 mmHg	40±13	37±12	66±17*	69±18†
pH	7.41±0.05	7.41±0.06	7.22±0.1*	7.2±0.1†
paO2 mmHg	184±67	270±87	189±73	258±101
Qs/Qt %	33.6±3	27.6±4	39.3±7.1*	37.6±8.5†
MPAPmmHg	30±6	27±4	40.±9*	35±7†
PVRI dynes/ s/cm-5/m2	445±143	390±122	525±223*	393±142
CI l/mn/m2	3.4±0.8	3.2±0.8	4.3±1 7*	4.6±1.6†
SvO2 %	66±8	68±6	73±8*	78±7†
NE pg/ml	573±259	536±244	1682±781*	1959±1061†

*: p<0.01 HC vs NC and †: p<0.01 HC+NO vs NC+NO (paired t tests). **CONCLUSION**: Acute HC induced a marked increase in PVRI and CI. Inhaled NO completely reversed the increase in PVRI, did not prevent the increase in CI and therefore partially reversed hypercapnia induced pulmonary hypertension.

A.110

EFFECT OF VECURONIUM PRIMING ON LUNG VOLUMES AND OXYGEN SATURATION IN MILDLY OBESE PATIENTS

RP Mahajan and AR Aitkenhead
University Department of Anaesthesia, Queen's Medical Centre, Nottingham, NG7 2UH,UK.

Background and goal of the study: A priming dose of vecuronium causes a significant reduction in lung function of non-obese, young adults, without any change in oxygen saturation (1). Because of markedly deranged chest wall mechanics, obese patients may be more vulnerable to the consequences of priming. This study addresses this issue in mildly obese (BMI<35) patients.

Materials and methods: Eight male patients(ASA 1-2) aged 22-44 yr (mean 31.1 yr), height 1.64-1.82 m (mean 1.73 m), weight 83-102 kg (mean 93.7 kg) and BMI 28.05-33 02 (mean 31.06) were studied in the anaesthetic room in the supine position. ECG and arterial oxygen saturation were displayed continuously. Total lung capacity (TLC), slow vital capacity (SVC), inspiratory capacity (IC), functional residual capacity (FRC), expiratory reserve volume (ERV) and residual volume (RV) were measured using a Morgan transfer test machine before and 3 min after the administration of vecuronium 0.01 mg kg^{-1} i.v.

Results: Significant reductions occurred in TLC, SVC, FRC, ERV and Spo_2 (Table); two patients required O_2 supplementation to improve their Spo_2 to > 90%. In all patients whose Spo_2 decreased by >4%, the post-priming FRC was reduced to values less than the pre-priming RV.

Table:Lung volumes(l) before and after priming. Mean(SD). *p<0.05; †p<0.01;#p<0.001.

	Before	*After*	*%Change*
TLC	5.80 (0.94)	5.27 (0.81)$^{\#}$	-8.82
SVC	4.03 (0.95)	3.60(0.79)†	-10.33
IC	3.27 (0.79)	3.43 (0.67)	+6.77
FRC	2.53 (0.59)	1.84 (0.41)$^{\#}$	-26.7
ERV	0.76 (0.42)	0.16 (0.21)$^{\#}$	-84.07
RV	1.77 (0.47)	1.67 (0.37)	-4.02
Spo_2	96.25(1.03)	92.50(3.46)*	-3.75

Conclusion: Priming with vecuronium 0.01 mg kg^{-1} in mildly obese patients causes a significant impairment of lung volumes and a significant decrease in oxygen saturation. The decrease in Spo_2 can be related to the reduction in FRC to a level that is less than the resting RV.

Reference:

Mahajan RP, Laverty J. Lung function after vecuronium pretreatment in young, healthy patients. *British Journal of Anaesthesia* 1992; 69: 318-319.

A.111

BI-LEVEL CPAP (BIPAP) REDUCES THE POST-OPERATIVE RESTRICTIVE PULMONARY SYNDROME IN OBESE PATIENTS AFTER GASTROPLASTY.

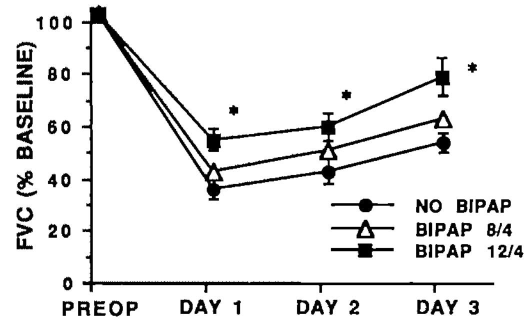
J Joris, T Sottiaux[1], JD Chiche, I Luten, M Lamy.

Departments of Anaesthesiology & Intensive Care Medicine, CHU LIEGE and ND de Grâce GOSSELIES[1], BELGIUM.

Background & goal of the study: Upper-abdominal surgery results in postoperative restrictive pulmonary syndrome. Bi-level CPAP (BIPAP) combines positive airway pressure during inspiration (IPAP) and expiration (EPAP) via a nasal mask. We studied the effect of BIPAP on pulmonary function in obese patients after gastroplasty.

Materials and Methods: 30 obese patients undergoing gastroplasty under general anaesthesia (isoflurane in 50% N_2O) were randomly assigned to one of 3 ventilatory support modes during the first 24 h postop: O_2 via a face mask, BIPAP (Respironics, Monroeville, PA) with IPAP and EPAP respectively set at 8 and 4 cm H_2O, or BIPAP set at 12 and 4 cm H_2O. The BIPAP groups received O_2 5 l/min directly in the nasal mask. Patients were asked to wear the mask at least 2 h every 3 h . All patients had the same chest physiotherapy and analgesic regimen (Patient-Controlled Analgesia with piritramide). Pulmonary function (forced vital capacity [FVC], forced expiratory volume in 1 sec [FEV1], peak flow [PF]) was measured (Controlair spirometer) before surgery (preop), 24 h after surgery, and on days 2 and 3. SpO_2 was also recorded at room air. Data (mean±SEM) were analyzed by ANOVA.

Results: Demographic data and preop respiratory function were similar in all groups. After surgery, FVC, FEV1, PF, and SpO_2 significantly decreased in the 3 groups. On day 1, FVC (Fig 1) and FEV1 were significantly improved (±50%) in the group BIPAP 12/4 as compared with no BIPAP. After the removal of BIPAP 12/4, these benefits were maintained, allowing a faster recovery of pulmonary function. No significant effects were observed for PF, and SpO_2. BIPAP 8/4 had no significant effect.



* p<0.05 as compared with no BIPAP.

Conclusion: These data suggest that prophylactic BIPAP 12/4 for only 24 h significantly reduces pulmonary dysfunction after upper-abdominal surgery in obese patients. An IPAP of 12 cm H_2O is required to be effective, possibly because of the decreased compliance of the respiratory system in obese patients.

A.112

EFFECT OF WEIGHT LOSS ON PULMONARY FUNCTION IN MORBIDLY OBESE PATIENTS.

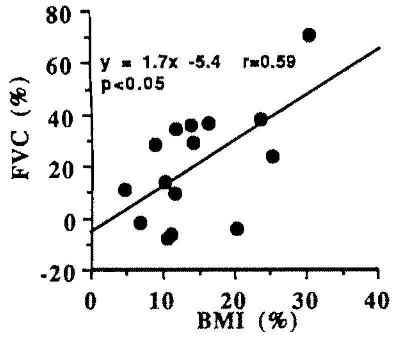
J. Joris, I. Frederick, C. Desaive*, M. Lamy .

Department of Anaesthesiology & Intensive Care Medicine,
Department of Surgery*
CHU LIEGE, B-4000 LIEGE, BELGIUM

Background & goal of the study: Obesity results in several respiratory pathophysiological changes.[1] Gastroplasty is efficient to treat morbidly obese patients with a body mass index [BMI = weight (kg)/height^2 (m)] superior to 40 kg/m^2 and allows a rapid and marked weight loss (±30-40 kg/year). We therefore investigated the effect of weight loss on pulmonary function.

Materials & Methods: After approval of our institution's Ethics Committee, 30 fully informed morbid obese patients who underwent gastroplasty had pulmonary function tests before surgery. One year and a half later, 15 (M=4, F=11) of these patients agreed for new respiratory testing. The following parameters were recorded: forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), peak flow (PF) using a Controlair® C 300 S spirometer, and SpO_2 (Datex Cardiocap®). Testing was carried out in semi-sitting position, and the average of three consecutive measurements was considered. Data, expressed as mean ± sem, were analyzed by paired Student's t test, and correlation between weight loss and changes in respiratory parameters was determined by linear regression.

Results: Before surgery, characteristics of the 15 patients were: age = 39 ± 3 yo, weight = 125.6 ± 7.2 kg, BMI = 45.1 ± 1.9. One year and a half later, weight was significantly ($P<0.05$) reduced to 84.7 ± 4.0 kg. Averaged weight loss was 40.9 ± 5.2 kg which correspond to a decrease of BMI of 14.7 ± 1.9. This weight loss resulted in a significant ($P<0.05$) increase in FVC (before: 2.95 ± 0.23 lit, after: 3.57 ± 0.33 lit), FEV1 (before: 2.36 ± 0.21 lit/sec, after: 2.77 ± 0.24 lit/sec), and PF (before: 308 ± 28 lit/min, after: 364 ± 35 lit/min). Increase in CV (% of preoperative value) was significantly correlated to weight loss. No significant changes in SpO_2 were observed.



Conclusion: This study demonstrates that weight loss results in improvement of pulmonary function. Interestingly, the increase in FVC, proportional to weight loss, was more pronounced and more clear cut than that of FEV1 and PF. These data provided scientific evidence to propose efficient treatment of obesity in case of respiratory problems.

Reference 1: BJA 1993;70:349-359.

A.113

NITROUS OXIDE INDUCES CENTRAL AND OBSTRUCTIVE APNEAS IN NORMAL SUBJECTS

L. Beydon, F. Lofaso, L. Heyer, L. Delaunay,
F. Goldenberg.
Dept of Anaesthesia, Hôpital Henri Mondor,
CRETEIL - France

Introduction: Nitrous oxide is commonly used as an analgesic agent, especially for labor pain. Like other anaesthetic gas, it depresses the level of consciousness. It therefore may depress respiratory command and induce central and obstructive apnea. This study was designed to answer this question.

Methods: 9 healthy male volunteers (29-43 years) without overweight and with no clinical history of sleep disease were studied in supine position, at 9 am, after an overnight fasting. Conventional sleep polysomnographic recordings (EEG, EMG, EOG) were performed in addition to continuous measurement of air flow, endtidal CO2, diaphragmatic EMG, and esophageal pressure. Patients were studied while breathing via a face mask, O2 100%, N2O 30% (N_{30}) and 50% (N_{50}) in O2, successively; during 30 minute periods.

Results: Total sleeping time (EEG) did not differ significantly between N_{30} and N_{50}. Subjects showed in average, 10 ± 3 respiratory events during each N2O period. Hypopneas with increased inspiratory resistance (HIR), central apneas, central hypopneas occurred under N_{30}, in 23%, 27%, and 50%, of cases, respectively , and in 23%, 26%, 47% of cases under N_{50}, (ns). Only 5 subjects showed HIR. Interestingly, those who experienced central apnea did not show HIR and vice versa. The duration of HIR correlated to the time spent in sleep stages 1 and 2, contrarily to central apnea wich sometimes occured in awake (EEG-assessed) condition. Awakenings terminated episodes of HIR in most instances, similarly to what has been described in sleep apnea syndrome (SAS).

Conclusion: N2O is a potent respiratory depressent, even in normal subjects. Each subject seems to respond either in an obstructive mode or central apneic one. Obstructive events were clearly related to the depth of sleep achieved under N2O in a way similar to what has been observed in SAS.

References:

Anesthesiology, 1984, 60:19-24.
Br J Anaesth, 1992, 68:27-31.

A.114

MECHANISMS OF ATELECTASIS FORMATION DURING GENERAL ANAESTHESIA

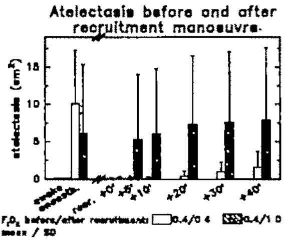
Hans Ulrich Rothen, Bengt Sporre, Greta Engberg, Göran Wegenius, Göran Hedenstierna

Departments of Clinical Physiology / Anaesthesiology and Intensive Care / Radiology,
University Hospital, Uppsala, Sweden

Backround and aim of study: *Atelectasis* is one of the reasons for an altered gas exchange during general anaesthesia [1]. However, the mechanism responsible for atelectasis formation and for the prolonged effect of a recruitment manoeuvre has not yet been elucidated [2]. The aim of this study was to determine the role of *resorption of gas* in poorly ventilated lung units [3] or behind closed airways after reexpansion of atelectasis.

Material and methods: We studied a consecutive sample of twelve adults with healthy lungs, scheduled for elective surgery.

Twenty minutes after induction of intravenous anaesthesia (Propofol, Fentanyl, Pancuronium) the lungs were hyperinflated manually. FIO_2 was either kept at 0.4 (group 1) or changed to 1.0 (group 2) immediately after the recruitment manoeuvre (random assignment; each group consisted of 6 subjects). The ventilation-perfusion relationship (V_A/Q) was estimated with the multiple inert gas elimination technique. Shunt was defined as $V_A/Q < 0.005$, and low V_A/Q as $0.005 < V_A/Q < 0.1$. Atelectasis was assessed by computed x-ray tomography. The amount of the dense areas (-100 to +100 Hounsfield units) was measured at end-expiration, in a transverse plane 1 cm above the top of the right diaphragm.



Results and discussion: (mean values are given) In group 1 the recruitment manoeuvre virtually eliminated atelectasis for at least 40 minutes (figure), reduced shunt from 7.2% of cardiac output to 1.3/2.3% (before and 20/40 minutes after recr.) and increased low V_A/Q from 6.7% to 11.3/8.3%. $P_{A-a}O_2$ decreased from 14.6 kPa (before) to 11.2 kPa (40 minutes after recr.; p = 0.028). In group 2 atelectasis reappeared within 5 minutes after recruitment, and there was no significant change in any of the measured parameters of V_A/Q. $P_{A-a}O_2$ is not given for this group because of the influence of change in FIO_2 *per se* upon this parameter.

Conclusion: During general anaesthesia in lung healthy patients, resorption of gas plays an important role in the recurrence of collapse in previously reexpanded atelectatic lung tissue. The reason for the instability of these lung units remains to be established.

References:

1 Gunnarsson L, et al: Influence of age on atelectasis formation and gas exchange impairment during general anesthesia. Br J Anaesth 1991, 66:423-432.
2 Rothen H U, et al: Recruitment of atelectasis druing general anaesthesia: a CT-study. Br J Anaesth 1993, 70(Suppl 1):A53.
3 Dantzker D R, et al. Instability of lung units with low V_A/Q ratios during O_2 breathing. J Appl Physiol 1975, 38(5):886-895.

A.115

Endoscopic transthoracic sympathectomy of the right-chest may cause severe hypoxemia.

Beno Rosenberg M.D., Yeshayahu Katz M.D., D.Sc. Eliahu Zisman M.D., Shlomo A. Isserles M.D.
Department of Anesthesiology, Rambam Medical Center and the Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Background: Endoscopic sympathectomy via a thoracic approach was recently introduced into practice (1). We present the cardio-respiratory effects of this procedure.

Materials and Methods: In nineteen ASA I-II patients, aged 16-35, heart rate, hemoglobin oxygen (O_2) saturation (SaO_2), end-tidal carbon dioxide (CO_2) concentration and intra-arterial blood pressure were monitored continuously. A double-lumen endobronchial tube was inserted and CO_2 was insufflated into the operated chest cavity to induce lung collapse and improve surgical field view. Arterial blood-gas samples were taken during two-lung ventilation before surgery (stage A), at one-lung ventilation (rt,stage B)(lt,stage D), during the period of two-lung ventilation when switching between the operated sides (stage C), and after operation (stage E).

Results: Left-lung ventilation induced a 71% (P<0.003) and 77% (P<0.001) decrease of PaO_2, compared to two-lung ventilation before surgery* and the calculated mean PaO_2 value at two-lung ventilation during and after surgery$^+$, respectively, and also, a concomitant decrease in SaO_2 values. Other blood-gas and hemodynamic parameters did not change throughout the operation.

Discussion: The profound hypoxemia may be due to compression of the great vessels in the right thoracic cavity. Means to overcome this hypoxemia are being currently investigated.

Stage	PaO_2 mmHg	SaO_2 (%)
A	256±114	98.8±0.9
B	194±94	96.4±4.7
C	328±161	98.6±1.1
D	75±29*$^+$	93.2±4.6*$^+$
E	303±152	98.6±1.1

Reference:

1. Byrne J, Walsh JN, Hedermans WP. - Br J Surg 77:1046-1049, 1990.

A.116

TITLE: Anaesthetic implications of transjugular intrahepatic portosystemic shunt in orthotopic liver transplantation.

AUTHORS: L. López-Olaondo, P. Monedero, J. de los Ríos, MJ Iribarren, F. Hidalgo, A. Sáez.
AFFILIATION: Anaesthesiology Department. Clínica Universitaria. School of Medicine. University of Navarre. Spain.

Background and goal of study: Transjugular intrahepatic portosystemic shunt (TIPS) has been recently used (1) as a way to control refractory variceal bleeding hemorrhage in cirrhotic patients before orthotopic liver transplantation (OLT). The intrahepatic portosystemic shunt is created via a transjugular approach to the hepatic veins using expandable, flexible metallic stents, under fluoroscopic and color Doppler sonography (2).
The goal of this study was to analyze both the influence of TIPS in preoperative haemodynamics, hepatic and renal function; and intraoperative blood products requirements and surgical time in OLT.

Patients & methods: We studied retrospectively 28 cirrhotic patients who underwent OLT. Ten patients with TIPS were compared with 18 patients (control group) without TIPS. Preoperative liver (bilirrubin and prothrombin time) and renal (urea, creatinine, urinary sodium and creatinine clearance) function tests and haemodynamics measurements (CI, SVRI, PVRI) were performed. Intraoperative hemoderivative requirements and surgical time were also measured.

Results & discussion: There were no significant differences between patients with or without TIPS in preoperative diagnosis, Child-Pugh status and hemostatic variables. Results are summarized in table 1. In spite of portal pressure reduction with TIPS, no preoperative changes in haemodynamics or renal and hepatic function were observed. Surgical time and blood product requirements were unchanged.

Table 1

	TIPS	Control
CI ($L.min^{-1}.m^2$)	4.8 ± 1.4	4.7 ± 1.6
SVRI ($dyn.seg.cm^{-5}$)	1374 ± 479	1284 ± 504
PVRI ($dyn.seg.cm^{-5}$)	127 ± 85	119 ± 47
Bilirubin ($mg.dL^{-1}$)	4.9 ± 3.2	4.4 ± 3.9
Prothrombin time (%)	53.6 ± 13.9	51.6 ± 21
Urea ($mg.dL^{-1}$)	39 ± 9	32 ± 16
Creatinine ($mg.dL^{-1}$)	0.95 ± 0.26	0.88 ± 0.23
Urinary sodium ($mM.L^{-1}$)	71 ± 46	55 ± 23
Creatin. clearan. ($mL.min^{-1}$)	75 ± 29	86 ± 45
Total surgical time (min)	428 ± 63	401 ± 68
Preanhepatic time (min)	194 ± 49	174 ± 44
PRBC (units)	4.7 ± 1.5	5.7 ± 3.4
FFP (units)	9.2 ± 2.3	9.1 ± 3.9
Platelets (units)	2.5 ± 4.3	1.9 ± 3.9
Cryoprecipitates (units)	2.7 ± 4.4	5.2 ± 7

Conclusions: TIPS did not modify our anaesthetic management of patients who underwent OLT.

References:

(1) Ring E.J. et al. Ann Int Med 1992; 116: 304-309.
(2) Conn H.O. Hepatology 1993; 17: 148-53.

A.117

TITLE: Effects of prostaglandin E_1 in orthotopic liver transplantation.

AUTHORS: P. Monedero, J. de los Ríos, F. Carrascosa, F. García-Pedrajas, A. Panadero.

AFFILIATION: Anaesthesiology Department. Clínica Universitaria. School of Medicine. University of Navarre. Spain.

Background and goal of study: The prostaglandins have a beneficial effect in a variety of animal models of hepatic failure due to toxins, hypoxia, ischemia and inmune mediation (1), and they have received increasing attention as promising, efficacious agents in the treatment of fulminant hepatic failure in humans. High doses of a prostaglandin E1 (PGE_1) analogue had proved to be useful in the treatment of hepatorenal syndrome (2). We studied the efficacy of prostaglandin E1 (PGE_1) to reduce liver and renal damage in orthotopic liver transplantation (OLT).

Patients & methods: We performed a prospective study (before-and-after trial) to evaluate the intra- and postoperative effects of PGE_1 in OLT. Eleven cirrhotic patients received PGE_1, 0.6 µg/kg/h continously, during the first three postoperative days, begining 10 minutes before reperfusion of the graft in the anhepatic phase of OLT. Patients receiving PGE_1 were compared with 17 previous untreated patients (control group). We evaluated intraoperative hemodynamic changes (CI, SVRI, PVRI), and postoperative renal (creatinine clearance, fractional Na^+ excretion) and hepatic (bilirubin, AST, ALT) function.

Results: Results are summarised in table 1 (mean ± SD). We found no statistically significant differences in the studied parameters (Mann-Whittney U test).

Table 1

	PGE_1	Control
CI ($L.min^{-1}.m^2$)	6.3 ± 1.7	6.6 ± 1.5
SVRI ($dyn.seg.cm^{-5}$)	1004 ± 309	855 ± 325
PVRI ($dyn.seg.cm^{-5}$)	100 ± 92	100 ± 60
Creatin. clear.1 (mL/min)	81 ± 41	83 ± 50
Creatin. clear.2 (mL/min)	105 ± 60	95 ± 48
F Na E 1 (%)	2.0 ± 1.7	2.2 ± 1.7
F Na E 2 (%)	2.1 ± 1.4	2.4 ± 1.3
Bilirubin 1 (mg/dL)	6.1 ± 2.1	6.4 ± 2.7
Bilirubin 2 (mg/dL)	4.4 ± 2.1	4.6 ± 2.5
AST 1 (mU/mL)	474 ± 388	597 ± 529
AST 2 (mU/mL)	647 ± 928	1191 ± 2002
ALT 1 (mU/mL)	516 ± 442	647 ± 595
ALT 2 (mU/mL)	817 ± 896	1416 ± 1902

Conclusions: PGE_1 did not affect intraoperative hemodynamics and postoperative renal and hepatic function.

References:

(1) Hepatology 1987; 7: 1184-8.
(2) J Hepatol 1990; 11: 153-8.

A.118

TITLE: INFLUENCE OF RESPIRATORY ALKALOSIS ON HEPATIC METABOLISM IN PATIENTS WITH HEAD TRAUMA

Authors: C. Ichai M.D., I. Baruch M.D., C. Samat M.D., D. Grimaud M.D.

Affiliation: Département d'Anesthésie-Réanimation, Hôpital Saint-Roch, 06006 NICE-cedex 1.

Background: The action of the liver to maintain the acid-base homeostasis (ABH) is yet admitted, but unknown in clinical situations (1, 2). The aim of this study was to evaluate the influence of respiratory alkalosis (RA) on the hepatic synthesis.

Materials & methods: After institutional approval and informed consent of the family, 10 patients with severe head trauma were included. Hypovolemia, hepatic and renal failure were non inclusion criteria. The protocol was divided into 4 phases : - A: pH = 7.40±0.05 mmHg, - B: 20 min of RA, - C: 3 hours of RA, - D: 24 hours of RA. RA was obtained by hyperventilation in order to have a pH > 7.45 and a change of the initial pH of at least 0.06. Alll patients were in controlled ventilation with neurosedation. They were monitorized with a capnograph (continuous FeCO2), arterial, Swan-Ganz and sushepatic catheters. The measured parameters at the 4 phases were: 1) arterial pressures, cardiac output, hepatic blood flow (continuous infusion of indocyanine cardiogreeen after a sushepatic catheterization), 2) arterial (A) and sushepatic venous (SHV) blood gases and electrolytes, 3) A and SHV urea, glutamine, lactate, pyruvate, 4) urinary urea at A and D, 5) ventilatory parameters. Statistical analysis was performed using a non parametric Wilcoxon test for paired data.

Results & discussion: In SVH blood, RA decreases the concentration of glutamine, but does not induce modification of urea. However, after 24 h, urinary urea excretion increases (Table I). RA increases also the arterial lactatemia. The experimental studies show that RA decreases the hepatic production of glutamine and increases those of urea and lactate (1, 2). Our results are in agreement with these data for the hepatic production of glutamine and lactate. The increase of urinary excretion expressed indirectly an increase in hepatic urea production.

Conclusion: RA induced by hyperventilation in patients with head trauma modulates the hepatic metabolic synthesis involved in ABH.

	Sushepatic Venous		*Arterial*	*Urinary*
	Urea mmol/l	Glutamine mmol/l	Lactate mmol/l	Urea mmol/24 h
A	4.86±1.02	275.2±26	1.46±0.2	138.4±21
B	4.5±0.86	210.8±15**	1.8±0.2**	
C	4.56±0.9	210.2±12**	1.75±0.2*	
D	4.53±0.88	233.4±29	1.53±0.1	178.4±27*

Table I : * p < 0,05, ** p < 0,01, moy±SEM

References: 1- ATKINSON DE. and al. *Curr. Topics Cell Regul.*, 21: 261-302, 1982

2 - HAUSSINGER D. and al. *Trends Biochem. Sci.*, 9: 300-302, 1984

A.119

CATECHOLAMINES PROFILE DURING ANESTHESIA IN DIABETIC PATIENTS WITH AUTONOMIC NEUROPATHY

D. LUGRIN, M.D., M. RAUCOULES, M.D., M. BEN MILED, MD, D. GRIMAUD, M.D.
Departement of Anesthesiology
Hôpital SAINT ROCH, 06006 NICE Cédex

Background and goal of the study : Existence of autonomic neuropathy is associated with an increase of perioperative morbidity in diabetic patients due to hemodynamic instability (1). The aim of this prospective study was to analyse simultaneously hemodynamic parameters and plasmatic catecholamine levels per operatively in diabetic patients with or without autonomic neuropathy.

Material and methods : 20 diabetic patients operated before 10 a.m. (cataract, vitrectomy) were included in the study : 10 patients with autonomic neuropathy (group A) were matched as for age, sex, body surface area with 10 patients without autonomic neuropathy (group B). Preoperatively a "blind observator" evaluated autonomic function : 1) parasympathic response by measure of heart rate (HR) during valsalva manoeuvre, deep breathing and standing up ; 2) orthosympathic by blood pressure responses to standing up and sustained hand grip. Anesthesia was induced by thiopental, fentanyl, atracurium and maintained with isoflurane, O2/N2O. The following data were registred : 1) mean arterial blood pressure (MAP) and HR ; 2) epinephrine (E) and norepinephrine (NE) dosages before induction (TO), 1 min after induction (T1), 1 min after intubation (T2), in the recovery period (T3).Hemodynamic and hormonal parameters were analysed in absolute values and in percentage of increase with reference to TO. Statistical analysis was perfomed by non parametric tests (p<.05, mean ± sem).

Results and discussion : There was no significant difference in hemodynamic parameters at TO, T1, T3. During intubation the increase in MAP was significatively less important in group A without NE modification (table I). In group A, NE levels remained steady during the 4 periods whilst in group B it decreased at induction and increased after intubation and in the recovery period (table II).

Conclusion : In dysautonomic diabetics abnormal vascular reactions exist during anesthesia most probably due to the absence of NE level fluctuations.

Reference : 1. Anesthesiology 70 : 591-597, 1989

	T1 - T0/T0		T2 - T0/T0		T3 - T0/T0	
	A	B	A	B	A	B
% MAP	- 8.8 ± 5.2	- 26 ± 10	+ 14.5 ± 5	+ 37.5 ± 8 *	- 15.6 ± 5	- 14.3 ± 3
% HR	- 4.9 ± 2.1	+ 5.3 ± 2	+ 4.9 ± 3	+ 10.5 ± 5.5	- 7.1 ± 5	- 4.1 ± 3
% NE	+ 7.6 ± 5.1	+ 10.6 ± 8	+ 5.9 ± 4	+130.8 ± 52 **	+ 21 ± 15	+ 73.5 ± 20

Table 1 : Percentage of variation (%) in MAP, HR and norepinephrine level (NE) with reference to TO .*p<.05 and ** p<.02 for intergroup comparisons.

	A				B			
	T0	T1	T2	T3	T0	T1	T2	T3
NE nmol/l	2.15 ±0.3	2.35 ±0.4	2.30 ±0.5	2.70 ±1.2	1.70 ±0.7	1.60 ±0.4	3.20 ±0.8	2.38 ±0.7

NS

** ** **

Table II : Norepinephrine levels (NE) in both groups. **p<.02 for intragroup comparisons.

A.120

HAEMODYNAMIC AND CATECHOLAMINE RESPONSES TO INDUCTION OF ANAESTHESIA IN DIABETIC AND NON-DIABETIC URAEMIC PATIENTS

M. Kirvelä, M. Scheinin*, L. Lindgren

Dept of Anaesthesia, IV Dept of Surgery,
Helsinki University Hospital, *Dept of
Pharmacology, Turku University, Finland

Attenuated cardiovascular responses to intubation have been seen in patients with diabetic autonomic neuropathy (DAN) (1). Plasma noradrenaline (NA) concentrations in DAN are reduced in both supine and standing position(2). We studied the pressor and catecholamine responses to tracheal intubation in 13 uraemic patients with diabetic nephropathy (group A), 12 uraemic non-diabetic patients (group B) and in 12 ASA 1 patients (group C).

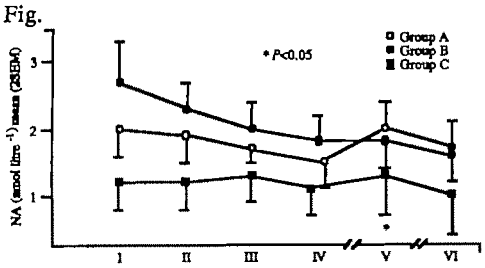
Patients and methods: The uraemic patients were undergoing renal transplantation and the patients in group C general surgery. A central venous cannula was inserted into the right atrium of the heart. Anaesthesia was then induced with fentanyl 2 $\mu g\ kg^{-1}$ and thiopentone 4 $mgkg^{-1}$ over 60 s. Muscle relaxation was with vecuronium and ventilation with 100% oxygen. Direct arterial pressures were recorded before induction (I), 60 (II),120 (III)and 180 s (IV) after thiopentone,and 60 (V) and 180 s (VI) after intubation. At these points, blood samples were drawn from the right atrium for plasma NA and adrenaline (A) assays (HPLC). Cardiovascular autonomic function tests were done two weeks later.

ANOVA for repeated measures with Duncan's test, unpaired *t*-test and Fisher's exact test were used for statistical analysis.

Results: Systolic arterial response to intubation was greater in group A than in groups B and C ($P<0.05$). The diastolic responses were similar in all groups. In group A, plasma NA concentrations increased significantly more than in group B and C after intubation (Fig.). The baseline NA and A levels were higher in uraemic than in ASA 1 patients. Abnormal autonomic function was apparent in groups A and B.

Conclusion: In uraemic patients with DAN, the systolic arterial pressure and NA responses to intubation were greater than in non-diabetic uraemic and ASA 1 patients. This may be due to impaired clearance of catecholamines as well as to higher baseline catecholamine levels possibly needed to maintain cardiac function.

Fig.



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A.121

QTc DISPERSION IN DIABETIC AND NON-DIABETIC PATIENTS WITH URAEMIA

M. Kirvelä, A. Yli-Hankala, L. Lindgren

Department of Anaesthesia, IV Dept of Surgery,
Helsinki University Hospital, Helsinki, Finland

Diabetic autonomic neuropathy (DAN) is associated with cardiac arrhythmias and sudden death (1). Prolongation of QT interval, a predisposing factor for arrhythmias, has been observed in DAN (1,2). Recently, increased QT dispersion (interlead variation) has been shown to correlate with arrhythmogenic risk better than a single lead QT interval (3). The prolongation of QT interval has been thought to be due to sympathetic imbalance. There is evidence, that QT dispersion reflects regional variation in ventricular recovery. Increased dispersion of recovery is known to be a predictor of ventricular arrhythmias. We compared the maximum heart rate corrected QT interval (QTc max), QTc dispersion and cardiovascular autonomic function in uraemic patients with diabetic nephropathy (group A), in uraemic patiens with other renal disease (group B) and in healthy subjects (group C).

Patients and methods: The patients in group A (13 pts) and B (13pts) were undergoing renal transplantation, the patients in group C (12pts) general surgery. QTc max and QTc dispersion were manually calculated from the preoperative 12 lead ECG. Autonomic function tests were done two weeks after the operation.

Kruskall-Wallis one way analysis of variance, unpaired *t*-test, Chi square and Fisher's exact test were used for statistical analysis.

Results: QTc dispersion differentiated the groups better than QTc max (Table). There were significantly more abnormalities in autonomic function tests in groups A and B than in group C, and less in group B than in group A. One patient in group A with preoperative QTc dispersion of 131 ms had an episode of ventricular fibrillation in the first postoperative morning at ICU.

Conclusion: In diabetic uraemic patients, increases in QTc dispersion and QTc max and severe autonomic neuropathy were observed. These may indicate high risk for cardiac arrhythmias. Also, uraemia itself seems to affect these parametres. Increased QTc dispersion is a valuable noninvasive measure for predicting severe postoperative cardiac arrhythmias in uraemic patients with autonomic neuropathy.

Table. Mean (SD)(ms).

Group	QTc max*	QTc dispersion**
A	498 (49)	100 (37)
B	462 (33)	51 (17)
C	433 (26)	29 (10)

*A vs C: $P<0.05$, **A vs B: $P<0.05$, A vs C: $P<0.001$
B vs C: $P<0.05$

References:
1. Kahn et al. J Clin Endocrinol Metab 1987; 64: 751-754
2. Ewing et al. Diabetic Medicine 1990; 7: 23-26
3. Day et al. Br Heart J 1990; 63: 342-344

A.122

ASSOCIATION CLONIDINE-ETOMIDATE AND INSULIN REQUIREMENTS IN DIABETICS DURING MINOR SURGERY

Marc Raucoules, Mehdi Boussofara, Didier Lugrin, Stephane Chave, Dominique Grimaud

Department of Anesthesia, Hôpital St-Roch, 06006 Nice Cedex 1, FRANCE

Background and goal of study: The goal of this study was to evaluate the effectiveness of the association of clonidine and etomidate on glycemic control and insulin requirements in diabetic patients during minor surgery.
Materials and methods: 20 adult diabetics for elective procedure (vitrectomy) before 10 a.m, were studied. Patients with preoperative glucose imbalance or autonomic neuropathy were excluded. By randomization group A (n=10) received cloninidine premedication (300 µg p.o.) 90 min prior to anesthesia. Anesthesia was induced and maintained with etomidate (0.3 mg.kg-1 and 0.01 mg.kg-1 min-1 respectively), fentanyl, vecuronium and N02/02. In group B (control group) patients were premedicated with flunitrazepam: 1-2 mg p.o.. Anesthesia was induced with thiopental (5 mg.kg-1) and maintained with N20/02, isoflurane, fentanyl and vecuronium. In both groups insulin was supplied by 1.25 units.h-1 in continous IV infusion and additional 7 units bolus of insulin were administered when blood glucose levels (BGL) exceeded 11.1 mmol.l-1. Glucose supply was 125 ml.h-1 of 5% glucose. BGL were measured every 15 min with glucose reagent strips during surgery and every hour during the 6 postoperative hours. Plasma catecholamine, cortisol, GH and aldosterone concentrations were measured prior to induction of anesthesia, 2 min after intubation, during surgical procedure, 2 min after extubation, 3 and 6 hours after the end of surgery. Comparisons were performed using a two-way ANOVA (p<.05).
Results and discussion: Both groups were comparable with regard to age, body weight, ASA-Status (II, III), duration of diabetes. The clonidine-etomidate group showed lower BGL (figure), plasma cortisol (p<.01) and catecholamine (p<.05) levels during and after surgery. Insulin requirements were strongly decreased during surgery (A: 5.9 ± 0.9 units, B: 16.2 ± 1.9 U; p<.01) and during the 6 postoperative hours (A: 8.5 ± 0.4 U, B: 33.5 ± 5.3 U; p<.01) as compared to group B.
Conclusion: The association of clonidine and etomidate permits an important decrease in insulin requirements in diabetics during minor surgery.

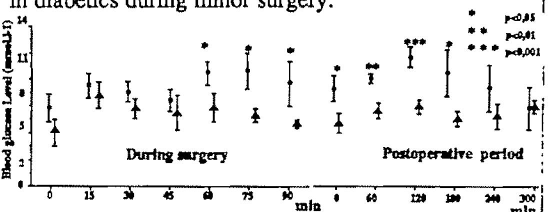

Fig: BGL (mmol.l-1) during and after surgery.
▲clonidine/etomidate ●control group

A.123

FORCED PERIOPERATIVE ERYTHROPOIESIS IN PATIENTS UNDERGOING MAJOR UROLOGIC PROCEDURES

BM Weiss, T Pasch, U Binswanger, K Gautschi, B Seifert

Departments of Anaesthesiology, Internal Medicine-Nephrology, Clinical Chemistry, and Biostatistics, University Hospital Zürich, CH-8091 Zürich, Switzerland

Background and goal of study: A prospective study was undertaken to evaluate if forced perioperative erythropoiesis, using recombinant human erythropoietin (rh-Epo) and/or iron, would reduce the requirements for homologous blood transfusion and/or enhance the recovery of red blood cells in patients undergoing elective major urologic procedures.
Materials and methods: After approval of the ethical committee and informed consent, patients undergoing cystectomy were randomized into Control and Epo-Iron [rh-Epo (Eprex*) 20'000 IU and iron (ferrum saccharat) 200 mg iv. on day 3 prior to surgery, rh-Epo 10'000 IU and iron 200 mg postoperatively, and rh-Epo 10'000 IU on day 1, 2, and 3 after surgery] groups. Patients undergoing radical or transvesical prostatectomy and nephrectomy were randomized into Control, Epo-Iron [rh-Epo 20'000 IU and iron 200 mg iv. on day 1 prior to surgery, rh-Epo 10'000 IU and iron 200 mg postoperatively, and rh-Epo 10'000 IU on day 1, 2, and 3 after surgery], and Iron [iron 200 mg iv. on day 1 prior to surgery and 200 mg postoperatively] groups. Patients with unstable cardiovascular or pulmonary diseases, neurological, haematological or coagulation disorders, and renal dysfunction were not included. Standardized anaesthetic technique, fluids and volume substitution, transfusion criteria, timing for laboratory analyses, and postoperative care were applied in all patients. Data were analysed by ANOVA for repeated measurements, Bonferroni-Dunn multiple groups comparison, and Student's t-test with Bonferroni's correction.
Results: Patients' characteristics, duration of operation, intra- and postoperative blood loss, and the crystalloids, colloids, and blood transfusion requirements were not different between cystectomy patients (n = 12), or between three groups of other patients (n = 29). Haemoglobin similarly changed in Control and in the treated groups. Significantly higher reticulocytes' count (P<0.03) was found in rh-Epo-treated patients until day 3 after surgery. Iron and ferritin levels were higher in Epo-Iron-treated cystectomy patients at day 1 (P<0.05), and day 1 and 7 (P<0.005) after surgery. Erythropoietin concentrations significantly increased in rh-Epo-treated patients until day 3, but showed a significant interaction ("cross-effect") at day 7 and 12 in cystectomy and in other patients, as well.
Conclusions: Attempt to force perioperative erythropoiesis did not influence the requirements for homologous blood transfusion, and only slightly enhanced the recovery of the iron and red blood cell status in patients undergoing major urologic procedures. Employed rh-Epo and iron dosage-time profile cannot be recommended for routine use. This treatment should be started earlier and administered longer than in this study.

*Eprex was supplied and the study was supported by Cilag AG, Schaffausen, Switzerland.

A.124

HORMONAL RESPONSES TO HYPOTENSIVE ANAESTHESIA

AM Matson, BL Loughnan, M Shaw and GM Hall*.

Northwick Park Hospital, Harrow, Middlesex, England.
*St. George's Medical School, Tooting, London, SW 17, England.

The majority of studies looking at the endocrine response to induced hypotension in humans have been performed during a period of surgical stress, it is therefore difficult to separate the effects of hypotension from those of surgery. Our aim was to investigate the endocrine response to hypotensive anaesthesia divorced from surgery and then during minor otological surgery, which induces minimal surgical stress.

We studied 24 ASA 1 or 2 patients aged 18 to 49 undergoing minor otological surgery of at least 1 hr. duration. Patients were anaesthetised using thiopentone,vecuronium and ventilated to normocapnia with N2O(66%), O2(33%) and isoflurane. Patients were randomised into three groups. Group C patients were monitored for 30 min. under anaesthesia maintaining Pe'Iso at 0.4-0.5% before the induction of hypotension to 60mm Hg (mean) using metoprolol 0.05mg/Kg and incremental isoflurane, when surgery was commenced. Group L patients received metoprolol prior to induction of anaesthesia and hypotension was achieved using incremental labetolol. Blood pressure was maintained at 60mm Hg for 30 min. before surgery. Group I patients were anaesthetised in the same manner as group L, hypotension was induced using incremental isoflurane.

Arterial samples for hormone analysis were withdrawn before administration of any drugs, following intubation, 15 and 30 min. after stabilisation of end-tidal isoflurane level (group C) or attainment of hypotension (groups L and I), 30 and 60 min. after the beginning of surgery and post-operatively at 30, 60, and 90 minutes.

There was no significant difference between the groups for any of the hormones studied. Cortisol, ACTH and AVP levels remained unchanged until the recovery period, when significant increases were observed. Aldosterone levels increased sequentially through presurgery and surgery samples. This was followed by a decline in the 60 and 90 minute recovery samples.

	Time 0	A/H 30	S 30	R 30
Cort.(nmol/l)	340.4 (254.9-454.4)	239.8 (179.7-320.2)	280.9 (210.4-375.0)	873.9 (654.6-1166.8)
ACTH (ng/l)	9.5 (6.2-14.6)	8.8 (5.8-14.6)	10.2 (6.6-15.6)	22.9 (14.9-35.2)
AVP (pmol/l)	5.6 (4-7.8)	4.5 (2.8-6.3)	6.1 (4.3-8.5)	17.2 (12.3-24.1)
Ald. (pmol/l)	205.4 (140.2-301)	386.4 (263.8-566.2	636.5)(434.4-932.6)	539.7 (368.3-790.8)

Geometric means for groups C, L and I combined (and 95% confidence intervals) of measured hormone levels before anaesthesia (time O), after 30 min. of anaesthesia +/- hypotension (A/H 30), after 30 min. of surgery (S 30) and after 60 min. recovery (R 30).

During normovolaemic hypotension with beta-blockade and isoflurane, plasma AVP played no role in blood pressure regulation and the importance of aldosterone is questionable. In addition, hypotensive anaesthesia failed to initiate any rise in ACTH or cortisol.

A.125

ARE THE IN VITRO CONTRACTURE TESTS AVAILABLE IN PATIENTS WITH VARIOUS NEUROMUSCULAR DISEASES ?

Pascal J Adnet, Benoit Tavernier, Toussaint Etchrivi,
Ghislain Haudecoeur, Renée Krivosic-Horber

Department of Anesthesia and Pharmacology, Univ. Lille, 59037
Lille cedex, France.

Background and goal of stuydy :The relationship between neuromuscular disease (NMD) and malignant hyperthermia (MH) susceptibility is usually assessed by the results of the in vitro halothane-caffeine (HC) tests (1). However, little was known about the physiological state of transected fibers from patients with NMD used for MH testing. To this end, we compared the contractile and electrophysiological properties of muscle fiber segments from patients with NMD and those obtained in MH family members biopsied during the same period of time.

Materials and methods : Twenty eight patients with NMD and 93 MH-related family (MHRF) patients were investigated with informed consent and approval by our Research Comittee.

During the MH diagnostic procedures resting membrane potentials (RMP), predrug twitch tension amplitude and 32 mM caffeine-induced contracture were recorded in each patient. Multiple comparisons analysis was provided using Scheffe's test.

Results and discussion : In NMD group the HC tests gave 1 positive, 6 equivocal and 21 negative results. Compared to the MHRF group (table1), muscle bundles used had lower RMP and lower predrug twitch tension amplitudes (P<0.05).

It is concluded that some of the results of the NMD group were obtained with damaged or more rapidly deteriorating muscle and should not be taken to indicate that the patients have or have not the genetic trait for MH. The HC test is not always adapted to myopathic muscle (and specially dystrophic muscle) and this could explain the lack of specificity of MH.

Table 1

	n	Twitch halothane (g)	Twitch caffeine (g)	32 mM caffeine (g)	RMP (mV)
MHS	15	2.1* (+/-0.8)	2.2* (+/-1.3)	8.8 (+/-4.1)	-79.1* (+/-4.7)
MHN	69	2.1* (+/-0.9)	1.9* (+/-0.8)	7.6 (+/-3.3)	-77.9* (+/-4.9)
MHE	9	1.7 (+/-0.7)	1.7 (+/-0.8)	7.1 (+/-3.1)	-79.8* (+/-5.6)
NMD	28	1.4 (+/-1.1)	1.4 (+/-1.2)	6.3 (+/-4.4)	-64.9 (+/-10.1)

Mean (± SD) values for halothane and caffeine twitch tension, 32 mM caffeine contracture and resting potentials from the 93 MH-related family (MHS : susceptible ; MHN : non susceptible ; MHE : equivocal) and the 28 patients with NMD

*statistically different from NMD (p<0.05).

Reference : 1) Heytens L et al : In vitro contracture tests in patients with various neuromuscular diseases. Br J Anaesth 1992 ; 68 : 72-75

A.126

THE EFFECT OF ISOFLURANE ANAESTHESIA ON GLUCOSE TOLERANCE IN SURGICAL PATIENTS

M. Knowles, J.P. Desborough, G.M. Hall,
Department of Anaesthesia, St. George's Hospital
Medical School, Cranmer Terrace,
London, SW17 0RE

Background: In vitro studies have shown that isoflurane and other volatile anaesthetic agents inhibit insulin secretion from pancreatic tissue (1). It is possible that isoflurane anaesthesia may impair glucose tolerance (2). We have investigated this using a 5 g ivgtt in healthy patients, both awake and following induction of anaesthesia, prior to the start of surgery.

Methods: 27 patients presenting for infertility surgery gave written informed consent. The results of 6 patients were excluded. Following premedication with morphine 10 mg and hyoscine 0.4 mg i.m., a central venous catheter was inserted via an antecubital vein, and baseline blood samples collected for blood glucose, serum insulin and plasma catecholamines. 5 g of glucose was given with blood sampling up to 15 min. 60 min after the bolus, anaesthesia was induced with fentanyl 2 μg/kg, and thiopentone. Vecuronium 0.1 mg/kg was used and the lungs ventilated with 70% N_20 in oxygen. Patients were randomised to receive either 0, 1 or 2 MAC isoflurane; 10 min after achieving the MAC value, the ivgtt was repeated. Results were calculated as the area under curve (AUC) for the 15 min insulin response.

Results: The glycaemic response to each ivgtt was similar in each group of patients. Within each group there was marked variation in the insulin responses. However, there was no significant difference between the three groups in the 15 min AUC in the awake ivgtt. The 15 min AUC response to the second ivgtt was significantly decreased in all groups ($p < 0.02$) compared with the awake ivgtt. n=7 in each group.

Insulin Response (AUC) mU/L x min Mean (SE)					
0 MAC		1 MAC		2 MAC	
awake	anaes	awake	anaes	awake	anaes
398 (87)	242 (44)	214 (22)	114 (22)	254 (40)	153 (47)

Conclusion: Glucose tolerance was decreased in surgical patients following induction of anaesthesia, but was not influenced by brief exposure to isoflurane.

References:
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2. Diltoer M, Camu F. Anaesthesiology 1988; 68: 880-6.

A.127

ANAESTHESIA FOR LIVER TRANSPLANTATION IN FAMILIAL AMYLOID POLYNEUROPATHY - A PRELIMINARY REPORT

Joaquim da Silva Viana, Helena Vieira, Carlos Bento, Sílvia Neves, Alexandre Linhares Furtado

Department of Anaesthesia and Department of Urology and Transplantation - University Hospitals of Coimbra, Portugal

Background - Familial amyloid polyneuropathy (FAP) is a heredofamilial type of amyloidosis. An abnormal protein, produced in the liver, has a decisive role to the clinical picture of the disease. Liver transplantation is now a promising experimental procedure to treat this genetic anomaly that is, at the moment, inevitably fatal.

FAP patients present, early in the course of the disease, an amyloid involvement of the cardiac conductive tissues and a serious autonomic nervous dysfunction [1]. In general surgery, others had previously reported "a substantial risk of developing sudden severe rhythm disturbances during anaesthesia" [2]. Regarding these specific cardiovascular problems and the absence of hepatic failure, FAP patients constitute a particular group to liver transplantation that deserves a special attention. The aim of this study is to evaluate the anaesthetic aspects of the transplantation of these patients

Patients and methods - Seven FAP patients, transplanted in our hospital in a seven month period, were studied (Group F). As control, we used eight cirrhotic patients transplanted in the same period of time (Group C). Acute hepatic failures or retransplantations were excluded

Results (mean +/- SD) and discussion:

Age: Group F (38.4 +/-9.6 years) was not different of Group C (38.5 +/-12.1 years) (p=ns)

Haemodynamics - Concerning MAP, CO and SVR, we were unable to detect consistent differences between the groups (p=ns). In heart rate, values observed in Group C were higher, during all phases of the procedure, than those of Group F ($p<0$ 05 or $p<0.01$) The most relevant clinical finding was the perception that FAP patients had difficulty to use their own mechanisms to compensate blood losses or even small increases in volatile anaesthetics.

Arrhythmias: FAP patients presented a good per-operative cardiac stability, but two patients developed, abruptly, short periods of ventricular tachycardia. Regarding the previous reports of arrhythmias in FAP, our study found an unexpected low incidence of minor events, but it support that FAP patients have a high tendency to malignant arrhythmias

Liver revascularization: No differences were observed between the Groups in the incidence (p=ns) and the magnitude (p=ns) of the haemodynamic depression The reperfusion syndrome seems to be independent of the pre-existing disease

Blood: Differences were observed between the groups, mainly related with the surgical difficulty. The needs of RBC, were 3.0 +/- 3.1 units in Group F and 13 9 +/- 14.5 units in Group C ($p<0.05$).

Time: The duration of surgery was 6:31 hours +/- 1:00 in Group F and 11:01 hours +/- 3:30 in Group C ($p<0.01$).

Conclusion: In the liver transplantation anaesthesia of FAP patients, the circulatory changes inherent to the disease, particularly rhythm disturbances, emerge as a major problem, needing a careful surveillance. However, in these patients, the surgical procedure tends to be shorter and with lower requirements of blood products than in cirrhotic patients.

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A.128

EVALUATION OF BISPECTRAL INDEX OF EEG FOR MONITORING OF ANESTHETIC DRUG EFFECT.

V BILLARD, PL GAMBUS, SL SHAFER, DR STANSKI
Department of Anesthesia, Stanford University, CA94305,USA

Background & goal of study: The analysis of EEG is widely used for measuring the effect of anesthetic drugs. Until now, most of the methods of analysis were based on frequency spectrum and power distribution in the different frequency bands. Bispectral analysis of EEG is a new approach that takes account of the degree of phase correlation between the different frequency components of the spectrum. Based on this, a bispectral index, "BIS" has been designed. The purpose of this study was to compare BIS with 2 spectral analysis parameters, spectral edge 95% (SE) and relative delta power (RDP).

Materials & methods: Retrospectively, we have analyzed the EEG recording of 31 adults included in previous studies in our lab and who had received an IV infusion of propofol, alfentanil, or midazolam at doses sufficient to achieve maximal EEG effect. Using the individual pharmacokinetic parameters and assuming the Hill equation described the relationship between effect-site concentration and EEG effect, a predicted effect has been calculated. Then, the best estimation of ke0 to describe the observed effect have been computed by a simple least squares method. The values obtained have been compared between the 3 parameters by a two-ways ANOVA.

Results: For the 3 drugs, the time course of BIS followed closely the one of SE, and more closely the one of RDP. When a biphasic effect was observed for SE or RDP, it often also existed for BIS. The observed value achieved (M ± CV) were as follows:

	Propofol (n = 12)	**Alfentanil** (n = 11)	**Midazolam** (n = 8)
BIS			
Base (%)	91.3 ± 4%	89.7 ± 5%	89.9 ± 5%
Min. (%)	44.2 ± 37%	35.5 ± 58%	44.0 ± 48%
ke0(min^{-1})	0.20 ± 35%	0.44 ± 55%	0.021 ± 28%
SE95			
Base (Hz)	20.9 ± 11%	21.6 ± 15%	19.3 ± 11%
Min. (Hz)	12.3 ± 24%	7.6 ± 29%	12.5 ± 26%
ke0(min^{-1})	0.21 ± 29%	0.54± 46%*	0.017 ± 18%
RDP			
Base (%)	32 ± 36%	21.3 ± 57%	28.4 ± 39%
Max. (%)	74.3 ± 13%	80.3 ± 12%	75.2 ± 13%
ke0(min^{-1})	0.27± 40%*	0.50 ± 36%	0.018 ± 31%

** : $p<0.05$ estimated ke0 with BIS vs. other parameters*

Discussion: At baseline, RDP showed a greater variability among patients and between groups compared to SE and BIS.

For the three parameters, the maximal EEG effect after propofol and midazolam were closed, whereas it was more pronounced after alfentanil.

Conclusion: BIS may be used for monitoring of anesthetic drug effect, as SE or delta power. The blood:CNS equilibration time estimation is moderatly longer using BIS than the other parameters for the drugs with fast equilibration.

A.129

PROPOFOL ATTENUATES GLUTAMATE TOXICITY MEDIATED BY NMDA RECEPTOR ON FETAL RAT HIPPOCAMPAL NEURONS

P. Hans, V. Bonhomme, G. Moonen, J. Collette

Departments of Anesthesiology, Physiology and Pathophysiology and Laboratory of Radioimmunology, University of Liège, CHR de la Citadelle, B-4000 LIEGE

The mechanisms responsible for the cerebral protective effect of anesthetic agents is still poorly understood. Available evidence indicates that excitatory amino acids are fully implicated in the neuronal damage that follows focal ischemia and traumatic brain injury. Hence, the present study was designed to investigate the effect of propofol (PF) on glutamate (GLU) induced neurotoxicity.

METHODS

Cultured rat hippocampal neurons were submitted to 10^{-4} M GLU, kainate (KA), and amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) for 20 h in the presence and in the absence of 5.6 10^{-3} to 5.6 10^{-5} M PF concentrations. Identical cultures were also exposed to 10^{-4} M GLU and N-methyl-D-aspartate (NMDA) for 10 min in the presence and in the absence of the same PF concentrations. In each experimental condition, the degree of neuronal damage, quantified by measuring neuron specific enolase (NSE) release into the bathing media, was compared with that observed in basic culture conditions. Results were analyzed using the one way analysis of variance and the Student's t test. $P < 0.05$ was considered signficant.

RESULTS

PF produced a concentration-dependent reduction in the NSE release by neurons submitted to both types of GLU exposure and to NMDA exposure. The sparing effect of PF was significant at 5.6 10^{-3} M and resulted in a 50 % reduction in NSE release. The toxicity elicited by KA and AMPA was unaffected by PF. PF and intralipid alone did not influence NSE release in the culture media.

DISCUSSION

Our results indicate that high PF concentrations attenuate significantly NMDA mediated GLU neurotoxicity in vitro. The presence of a phenyl structure common to PF and other non competitive NMDA antagonists could suggest that PF acts on the phencyclidine recognition site at the NMDA receptor. Finally, it remains to be seen to what extent this protective effect can be confirmed in vivo before suggesting PF could be of therapeutic value in pathological states involving excessive GLU release.

A.130

EFFECTS OF POTENT INHALATIONAL AGENTS ON Ca^{++} TRANSPORT IN SYNAPTIC PLASMA MEMBRANES FROM RAT BRAIN.

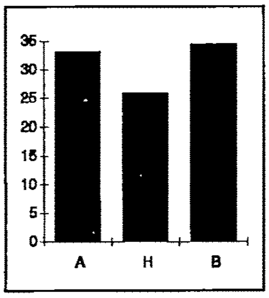
J-L. Horn, J.J. Franks, S. Brezinski, S. Milatovic and G. Singh.

Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee, USA.

Background and goal of study: Intracellular calcium as a second messenger plays a major role in the release of neurotransmitter into the synaptic space.[1] Therefore, alterations in regulation of the 10^4 fold Ca^{++} gradient across cellular membranes may be involved in the production of the anesthetic state. We have already observed that plasma membrane Ca^{++} pump activity, mainly responsible for the maintenance of that transmembranal gradient[2], is inhibited in synaptic plasma membranes (SPM) from rat brains exposed to anesthetic concentrations of halothane (H).[3] The goal of the present study was to evaluate the alteration of the Ca^{++} pump activity in cerebral SPM exposed ***in-vitro*** to bis(2,2,2-trifluoroethyl)ether (B), a fluorinated derivative of diethyl ether which possesses physico-chemical properties of halogenated anesthetics (e.a. hydrophobicity) without producing any anesthetic effect.

Materials and methods: Six groups of an average of 10 male Sprague-Dawley rats were decapitated. SPM were isolated from their cerebra by subcellular fractionation. Aliquots of SPM were incubated for 1 hour at 37°C with air (A) as control, with H or with B at relevant clinical concentrations (1.3 MAC) determined by the Meyer-Overton rule. Ca^{++} pump activity was measured by the accumulation of ^{45}Ca^{++} in everted SPM vesicles. Statistical significance was inferred at $P<0.05$ (repeated measures ANOVA).

Results and discussion: The figure below illustrates ^{45}Ca^{++} accumulation (nmoles) per mg of protein of cerebral SPM during one hour exposure to A, H or B. As demonstrated earlier, H depressed the Ca^{++} transport in SPM. B did not alter Ca^{++} transport significantly compared with controls. Those findings reinforce the hypothesis of a possible specific alteration in Ca^{++} regulation processes related to the production of anesthesia.



Conclusions: Specific interference with calcium homeostasis mechanisms in neuronal membranes (Ca^{++} pumping) by anesthetic concentrations of H and the absence of significant effect induced by B (a convulsant agent with similar physico-chemical properties of H) provides evidence for involvement of plasma membrane Ca^{++} ATPase as a possible site of action for anesthetic state produced by halothane.

Supported by NIH grant GM46401 and the Study Center for Anesthesia Toxicology. We thank Anaquest for the supply of the compound B.

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A.131

Title: BRAIN PERFUSION DURING CEREBRAL ISCHAEMIA PROTECTS NEURONS IN RATS

Authors: HJ Schmitt, M.D., GR Barth, P Thierauf*, M.D.
Afiliation: Institutes of Anaesthesiology and Pathology*, University of Erlangen-Nuremberg, 8520 Erlangen, FRG

Introduction: Magnesium (Mg) has been shown to prevent postanoxic neuronal cell death in-vitro[1]. Aim of this study was to investigate possible protective effects of Mg enriched solution during ischaemia by brain perfusion in-vivo.

Methods: Following animal care committee approval, male Wistar rats (450-500g) were anaesthetized with halothane and ventilated to maintain normoxaemia and normocapnia . After insertion of an arterial and venous line right external carotid artery was dissected, catheterized with a 24G canule and connected to a syringe pump. After steady state of 20min, ischaemia was induced by unilateral carotid occlusion combined with hypotension to 30±3mmHg for 30min[2]. During ischaemia right brain was perfused via external carotid in group M (n=7) with 1,5ml normothermic(37°C) Mg enriched solution (NaCl 37mmol/L, KCl 1.5mmol/L, $MgSO_4$ 30mmol/L, mannitol 180mmol/L, NaH_2PO_4 10mmol/L), in group N (n=4) with normothermic NaCl 0.9% 1,5ml at a rate of 3ml/h respective. Group I (n=2, ischemia without perfusion) and group C (n=7, no ischemia, no perfusion) served as control. Body and brain temperature were kept at 37±5°C.Blood glucose level was controlled pre- and postischemic.After 2h of reperfusion, rats were anaesthetized and the brain perfusionfixed. For electronmicroscopy hippocampus was cut in 500µm slices. Neuronal damage of the complete CA1 region was verified by a blinded investigator according to the following scale:[3] 0 = no damage, I = chromatolysis, II = swelling of astrocytes, III = vacuolization. Statistical analysis was performed with the χ^2 - test, $p<0.05$ was considered significant.

Results: Histologic outcome is shown in the table. Neuronal damage was significant ($p<0.0001$) different between all groups, with the lowest damage in group M out of the ischaemic animals.

Table:		damage score	0	I	II	III
Number of	group	M	8	128	155	46
cells		N	41	38	177	192
(means)		I	53	12	56	243
		C	319	62	34	2

Diskussion: This in-vivo study demonstrates brain protection by brainperfusion with magnesium enriched solution and confirms in-vitro neuronal protective effects of magnesium.

References: 1. Science 220:536-537, 1983
2. Stroke15:704-710,1984
3. Acta Neuropath (Berl) 26:329-344, 1973

A.132

INTRA- AND POSTOPERATIVE EFFECTS OF INFORMATION PRESENTED DURING SUFENTANIL ANESTHESIA

B.Verhamme*, M. Schlenga*, J. De Houwer**, P. Eelen**,
R. Demeyere*
Departments of Anesthesiology* and Psychology**, Catholic
University of Leuven, Belgium.

Introduction : Studies suggests that auditory processing proceeds further during sufentanil anesthesia (1). Patients scheduled for elective coronary artery bypass grafting (CABG) were investigated to see if they preserve an unconscious memory and if information presented to these anesthetised patients could be exploited to achieve a better postoperative outcome.

Methods : After institutional ethics committee approval, 48 male patients scheduled for elective CABG, with an acceptable left ventricular function and free of hearing or neurological disorders were studied. In a preoperative visit, verbal informed consent was obtained and preoperative mood and anxiety were assessed. All patients received standard invasive monitoring. After premedication with lorazepam (0.06 mg/kg) one hour before operation, anesthesia was induced with etomidate 0.25 mg/kg and sufentanil 1-1.5 µg/kg preceded by pancuronium or vecuronium 0.02 mg/kg. The lungs were mechanically ventilated with air and oxygen ($FiO2=0.6$). Anesthesia was maintained with further increments of sufentanil 1-2 µg/kg to a mean total dose of 17.8 µg/kg and with boluses of midazolam per 1.5 mg to a mean total dose of 8.6 mg. Nitrous oxide and volatile anesthetics were not used. Post induction all study patients were connected to a portable auto -reverse casette player via ear-phones. There were 3 tapes, adapted to 3 stages of the operation (before cardiopulmonary bypass (CPB), hypothermia phase and post CPB) for every patient. The patients were randomised in two groups : half of the patients received therapeutic suggestions with a background of appropriate relaxing music, and for the control subjects visually indistinguisable blank tapes were used. Furthermore half of the experimental and half of the control subjects were presented a list of nonsense words at the last tape, the others received another list of nonsense words. (In fact there were 8 possible situations). Standard hemodynamic monitoring was performed per- and postoperatively until discharge from intensive care unit (ICU) and at five fixed events (post induction, after sternotomy, before and after CPB, end of operation) blood samples for catecholamine dosages and sufentanil plasma levels were taken.

Results : Eight patients were excluded due to problems of diverse origin. Extracorporeal circulation time, aortic clamping time and reperfusion time tended to be smaller in the suggestion group. Peroperatively the suggestion group seemed to be hemodynamically more 'relaxed', which was concluded from significantly lower mean arterial pressure, left ventricular stroke work index and lower epinephrine levels. There was a significantly higher need for sufentanil in the non-suggestion group before CPB as well. No differences were found on heart rate or norepinephrine levels. The time to extubation, ICU and hospital stay, analgesic-and sedation need in ICU was equivalent as well. No differences were found in postoperative mood and anxiety, assessment of recovery by nurses at ICU, or preference and recognition for presented and non-presented words. However, above chance recognition was observed in the non suggestion group.

Conclusion : High doses of sufentanil with boluses of midazolam provide a safe anesthesia and good amnesia for elective CABG. Therapeutic suggestions can be used peroperatively to reduce the intra-operative stress response and the need for sufentanil which could be of benefit in patients who are not tolerating high doses, especially before CBP. Therapeutic suggestions have no influence on postoperative recovery and outcome.

Reference : (1) : J Cardiothorac Vasc Anesth 5: 577-583, 1991.

A.133

PROPOFOL AND THIOPENTAL INDUCTION: EEG AND CLINICAL ENDPOINTS

O.H.G. Wilder-Smith, P. Ravussin, A. Borgeat,
D. Bettex, P. Desplands
Departments of Anaesthesiology & Neurology
Geneva & Lausanne University Hospitals, Switzerland

Introduction and Aims

The potency relationships between CNS pharmacodynamics and ability to modulate CNS processing for intravenous anaesthetics are of increasing interest. The aim of this study is to investigate these relationships for EEG and clinical events during infusion induction of anaesthesia with propofol or thiopental.

Patients and Methods

After institutional and informed patient consent, we studied 15 patients undergoing elective prolapsed intervertebral disc surgery. They were randomly assigned to receive an infusion of 55mg/kg/h of thiopental (TH; n=8) or 30mg/kg/h of propofol (PR; n=7) for induction of anaesthesia. Before induction, continuous 8 channel EEG monitoring was started. *Endpoints:* time in minutes (t), cumulative dose in mg/kgbw (cd) & the PR:TH dose ratio (dr) to: loss of verbal contact (LVC), dropping an infusion bag held in the right hand (DIB), loss of reaction to a painful stimulus (LRP) (transcutaneous electric stimulation at twice the pain tolerance threshold); appearance of beta, theta and delta EEG rhythm, first appearance of burst suppression (3 sec interval) Any EEG reaction to laryngoscopy and intubation (L&I), which took place after the appearance of burst suppression, was recorded. The infusion was stopped after the appearance of burst suppression, and normal anaesthesia continued. Results: medians; signific: p<0 05 (Mann-Whitney U/Wilcoxon).

Results and Discussion

	beta	**theta**	**delta**	**burst**	**lvc**	**dib**	**lrp**
t-PR	1.5	3.7	4 0	8	3.5	3 8	9.6
t-TH	1.5	4.7	4 1	12.6	4.19	4.0	6.0
cd-PR	0.75	1.5	2 00	4.00	1.75	1.88	3.00
cd-TH	1.38	4.28	3.77	11.50	3.76	3.03	5.50
dr	0.55	0.35	0.53	0.35	0.47	0.62	0.55

Two patients in the PR, and four in the TH group showed EEG reactions (loss of burst suppression) to L&I. The differences between between the two groups for cd were significant for burst suppression and loss of verbal contact.

Conclusions

The potency ratios for the endpoints lie within the range of clinically accepted values. Propofol is particularly potent for the induction of burst suppression, with fewer patients showing an EEG reaction to L&I during it.

A.134

EFFECTS OF CHRONIC ADMINISTRATION OF DIAZEPAM ON THE SEPTUM AND AMIGDALOID AREAS OF RAT

Lasheras A, Carrera J, Carassiti M, Monedero P, Arroyo JL.
Departments of Anesthesiology. University Clinic. Faculty of Medicina. University of Navarre. Spain.

Background and goal of study: Previous studies have eMphasised the importance of de amygdala and septum in the therapeutic actions of benzodiazepines (BZ). However is difficult to know to what extent the neuronal alterations correspond to a direct or to an indirect action of BZD.
The purpose of this study is to evaluate the effect of chronic administration of diazepam on the amygdala and septum areas.

Materials and methods: 24 rats (wistar) were divided in to two groups of 12 rats each. Group I received Diazepam 1 mg/kg/24 h. i.m. The group II (control) received 1 ml of saline/24 h. i.m.
After 120 days of diazepam administration, the rats, under deep anesthesia, were transcardially perfused with 500 ml of saline, followed by 800 ml of buffered formalin (10%). Once removed, brains completed their fixation in formalin. The brain block was processed for paraffin embedding and serial coronal sections were obtained (7 μm).
To evaluate the state of the amygdala and septum a neuronal count and caryometry were carried out. NEURONAL COUNT.- In rats, 10 sections per neuron, regularly distributed from one end to the other of the corresponding nucleus, were counted. Only neurons with a prominent nucleolus were taken into account. CARIOMETRY.- The nuclear area was measured by a manual method: the contours of the nuclei (100 per each nucleus) were drawn (x3.800) and then outlined with a digitalizer compled to a Hewlet Packard computer that provided the area, the mean, the standard deviation, etc. The numerical date were analyzed statiscally.

Results and Conclusions: We found a clear significant reduction in the number of neurons in the amygdala (27,2% to; $p < 0{,}01$) and septal areas (22,9%; $p < 0{,}01$) of group I en relation of group II. There was also a significant ($p < 0{,}01$) reduction of the nuclear size of amigdaloide and septal nucleus in the group I (29,4% to and 48,9% to respectively) in relation to group control.
Our results showed a neuronal loss after chronic administration of Diazepam. These changes that appear in the different cerebral centres after administration of Diazepam suggest a basis for future studyes in humans.

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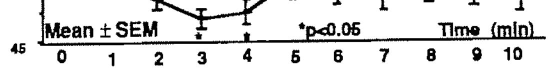
A.135

ROLE OF HYPOTENSION IN THE CEREBRAL HEMODYNAMIC EFFECTS OF SUFENTANIL AND FENTANYL

S. JAMALI, P. RAVUSSIN, D. GOUTAILLER, F. PARKER, C. ECOFFEY

Département d'Anesthésie, Université Paris-Sud, Hôpital de Bicêtre, Le Kremlin Bicêtre, France

Background & goal of study: The effects of opioids on intracranial pressure (ICP) and cerebral perfusion pressure (CPP) are controversial. Fentanyl (F) and sufentanil (S) have been found to increase ICP in severe head trauma patients (1). One of the mechanisms suggested to explain this response is a systemic hypotension causing cerebral vasodilatation which increases ICP. The aim of this study was to analyse the effects of F and S on the cerebral hemodynamics in the absence of hypotension.
Material and methods: This randomized and double-blind study involved 31 patients scheduled for supratentorial craniotomy. After premedication with 100 mg of hydroxyzine a general anesthesia was induced with 2 mcg/kg of fentanyl, 1.5 mg/kg of lidocaine, 5-7 mg/kg of thiopentone and 0.1 mg/kg of vecuronium. After endotracheal intubation a lumbar spinal catheter was inserted to measure the cerebrospinal fluid pressure (CFP) which accurately reflects ICP if CSF circulation is free. Anesthesia was maintained with 0.3-0.7 MAC of isoflurane. After stabilisation of the mean arterial pressure (MAP) at its baseline value level (± 10 %) without any noxious stimulus, 0.8 mcg/kg of S in the first group (n = 11), 4.5 mcg/kg of F in the second group (n = 11) and a placebo of 0.9 % NaCl in the third group (n = 9) were injected. MAP was maintained at its baseline level (± 15%) with isoflurane or incremental doses of phenylephrine (50-100 mcg). End - tidal CO2 (ET CO2) was maintained between 32 - 35 mmHg. MAP, CFP, heart rate (HR), and ET CO2 were recorded every minute during the next 10 min. Data were evaluated for statistical analysis using two-ways and one-way ANOVA tests.
Results: All groups were identical for age, weight, baseline MAP, CPP, HR. No difference was found in ICP between groups during the study period. CPP was significantly lower in group S vs F and placebo groups at the 3rd and 4th min (figure). HR (initial values 66 ± 9, 71 ± 14, 77 ± 15 beats/min {mean ± SD} respectively in the groups S, F and placebo) significantly decreased in the F (13 %) and S (20 %) groups vs placebo group during the study period ($p < 0.05$). To maintain MAP, S and F groups required 170 and 95 mcg of phenylephrine respectively. Four patients in each of the groups S and F required atropine sulfate because of bradycardia <45 beats/min.
Conclusion: Even in the absence of systemic hypotension, fentanyl ensures better cerebral hemodynamic stability than sufentanil when given for craniotomy in space-occupying lesions.
Reference: 1) RJ Sperry et al. Anesthesiology 77: 416-20, 1992.



A.136

Effects of sufentanil and fentanyl on the cerebral hemodynamics after a noxious stimulus

S. JAMALI, P. RAVUSSIN, M. BONNAFOUS, P. DAVID, C. ECOFFEY

Département d'Anesthésie, Université de Paris-Sud, Hôpital de Bicêtre, Le Kremlin Bicêtre, France

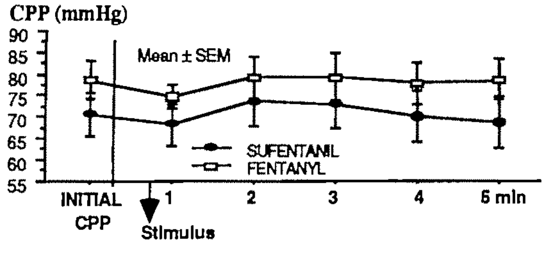
Background & goal of study: The effects of opioids on intracranial pressure (ICP) and cerebral perfusion pressure (CPP) are controversial. Fentanyl (F) and sufentanil (S) have been found to increase ICP in severe head trauma patients (1) but not in healthy volunteers (2). The aim of this study was to analyse the effects of fentanyl versus sufentanil on the cerebral hemodynamic response for a well-defined noxious stimulus.

Material and methods: 22 patients were included in this randomized and double-blind study. After premedication with 100 mg of hydroxyzine a general anesthesia was induced with 2 mcg/kg of fentanyl, 1.5 mg/kg of lidocaine, 5-7 mg/kg of thiopentone and 0.1 mg/kg of vecuronium. After endotracheal intubation a lumbar spinal catheter was inserted to measure the cerebrospinal fluid pressure (CFP) which accurately reflects ICP if CSF circulation is free. Anesthesia was maintained with 0.3-0.6 MAC of isoflurane. Then 0.8 mcg / kg of sufentanil in group 1 (SG; n = 11) and 4.5 mcg/kg of fentanyl in group 2 (FG; n = 11) were injected. After a stabilisation period of 20 min, a Mayfield skull-pin head holder was applied, which is a well-defined and reproducible noxious stimulus. The MAP, CFP and HR were continuously monitored and recorded before the injection of opioids (initial), before the noxious stimulus, and every min during the following five min. End - tidal CO2 was maintained between 32 - 35 mmHg. CPP was calculated as MAP-CFP. Data were evaluated for statistical analysis using two-ways ANOVA and Student's t tests.

Results: The two groups were identical for age, weight, baseline MAP, CPP, HR. No difference was found in CFP or CPP (figure) between groups all over the study. HR (initial values 67 ± 17 and 68 ± 8 beats/min as mean ± SD) was significantly lower (15 %) in the SG vs FG group after the stimulus ($p < 0.05$). It decreased by 10 % in the SG group after the stimulus vs initial value ($p < 0.01$).

Conclusion: Sufentanil as well as fentanyl in patients with a space-occupying cerebral lesion preserve adequately the cerebral hemodynamic response after a well-defined noxious stimulus.

Reference: 1) RJ Sperry et al. Anesthesiology 77: 416-20, 1992. 2)N Mayer et al. Anesthesiology 73: 240-3, 1990.



A.137

RESPONSE OF CEREBRAL BLOOD VOLUME TO CHANGES IN PaCO2 IN CHILDREN WITH CONGENITAL HEART DISEASE

D.N.Hunter, A.D.Edwards*, I Roberts*, A.N.Redington.
Departments of Anaesthesia & Paediatric Cardiology, Royal Brompton National Heart & Lung Hospital, and *Royal Postgraduate Medical School, London, England.

Profound changes in PaCO2 are often used in the management of infants following surgery for congenital cyanotic heart disease in order to manipulate pulmonary vascular resistance. However, little is known about the effect of these manipulations on the cerebral circulation in this context, and particularly whether neurological outcome is adversely influenced. We postulated that infants with cyanotic heart disease may have a lesser cerebral blood volume reactivity to PaCO2 (CBVR) compared to those infants with a normal PaO2.

Method. Six patients were studied, median age 9.2 months (range;2-17), with parental consent during the course of routine cardiac catheterisation. Patients were anaesthetised, intubated, and ventilated in oxygen and air (FiO2 0.5) with isoflurane adjusted to an end-tidal concentration of 1%. The optodes of a NIRO 500 (Hamamatsu UK) near infrared spectrometer (NIRS) were attached to the left temple of the patient 4 cm apart, and covered with an infrared occlusive drape. At the end of the catheter procedure the PaCO2 was allowed to rise over a 15 minute period. During this time NIRS data was averaged and recorded every 5 seconds together with the mean blood pressure from an arterial line, and the end tidal carbon dioxide level (EtCO2). Arterial blood gases (ABG's) were taken every 5 minutes. Data analysis using a computer was carried out later. The ABG's results were used to ensure linearity of EtCO2 data. CBVR in mls/100g brain tissue/kPa was then calculated using a method described previously (1).

Results; are expressed as median (range). PaO2 during the study periods was 10.5 (5-40) kPa; blood pressure was stable thoughout the study period in all patients 58 (40-65) mmHg; the rise in PaCO2 achieved was 0.74 (0.6-1.5) kPa; and CBVR 0.62 (0.28-0.8) ml/100g/kPa.

There was a negative correlation between PaO2 and CBVR ($r = 0.96$, $p<0.01$).

The CBVR values obtained here in children under the age of 18 months compare well with those found previously in term infants (CBVR = 0 5 ml/100g/kPa)(1). Contrary to our original premise, those children with severe cyanotic congenital heart disease tend to have a higher CBVR than those with a normal PaO2

Ref: Response of cerebral blood volume to changes in arterial carbon dioxide tension in preterm and term infants. J.S.Wyatt et al. Pediatr Res 1991;29(6):553-557.

A.138

COMPARISON OF BUPIVACAINE AND ROPIVACAINE METABOLIC EFFECTS IN RAT CARDIAC SKINNED FIBERS

François Sztark, Olivier Tueux, Jean-Pierre Mazat, Philippe Dabadie

Laboratoire d'Anesthésiologie, Hôpital Pellegrin and Université Bordeaux II, 33076 Bordeaux Cedex, France.

Background and goal of the study: The effects of local anaesthetics on mitochondrial energy metabolism lead to a decrease in ATP synthesis and could in part explain the bupivacaine-induced myocardial depression [1]. Ropivacaine is structurally related to bupivacaine. However ropivacaine is prepared as an S(-) isomer and its lipid solubility is intermediate between that of lidocaine and that of bupivacaine [2]. In addition, ropivacaine may be less cardiotoxic than bupivacaine. The goal of this study was to compare the effects of ropivacaine and bupivacaine on mitochondrial respiration in rat cardiac skinned fibers.

Materials and methods: Subendocardial left ventricular fibers were skinned in a relaxing solution containing saponin (50 μg/ml). The oxygen consumption rate (in nmol O/min/mg dry weight) was measured polarographically using a Clark electrode. Isolated mitochondria were obtained from rat heart. The activities (in nmol of products/min/mg protein) of the enzymatic complexes of the respiratory chain were determined using spectrophotometric methods.

Results and discussion: Bupivacaine and ropivacaine produce an inhibition of the respiration rate of mitochondria in skinned fibers. The depressant effect of bupivacaine is 43% greater than that of ropivacaine. On the contrary, enzymatic procedures show an inhibitory effect of both local anaesthetics on the isolated complex I (NADH ubiquinone reductase) with the same sensitivity (50% inhibition with 0.36 and 0.38 mM of bupivacaine and ropivacaine respectively). These results could be explained by the relatively greater lipid solubility of bupivacaine. This property may allow bupivacaine to penetrate the mitochondrial membrane more than ropivacaine.

Conclusion: High lipophilic local anaesthetics inhibit mitochondrial energy metabolism [3]. Bupivacaine appears in this study more toxic than ropivacaine for mitochondrial energy metabolism. The less cardiotoxicity of ropivacaine could be in part explained by these results.

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A.139

ARTERIAL AND PERIPHERAL VENOUS CONCENTRATIONS OF BUPIVACAINE FOLLOWING COMBINED SCIATIC AND FEMORAL 3-IN-1 BLOCKS

Misra U., Pridie A.K., Bower S., Stafford M.A., Halshaw J.
City Hospitals, Sunderland, U.K.

Background and goal

The importance of the site of blood sampling in the determination of plasma concentrations of local anaesthetics has been demonstrated by Bachmann et al[1] after epidural anaesthesia. Nolte et al[2] compared lignocaine levels in arterial, central venous and peripheral plasma after intravenous injection. The aim of this study was to compare arterial and venous concentrations of bupivacaine following combined sciatic and femoral 3-in-1 block.

Patients and methods

Fifteen consecutive patients undergoing knee replacement surgery were administered combined sciatic and femoral 3 in 1 blocks with 45 ml 0.5% plain bupivacaine solution using a nerve stimulator and 100mm long insulated Pole needle. Arterial and peripheral venous concentrations of bupivacaine were estimated at 5, 10, 15, 20, 25, 30, 45, 60, 75 and 90 minutes. The difference was expressed as a percentage of the arterial level.

Results

The mean difference was 14.63% (N=142, SEM 1.68, 95% confidence interval 11.30 - 17.96, P(μ=0)<0.0001).

Conclusion

In spite of the slow absorption of local anaesthetic solutions from the anatomic space after combined sciatic and femoral 3 in 1 blocks[3], peripheral venous concentrations of bupivacaine do not truly reflect the arterial concentration and hence the toxicity.

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A.140

TITLE: PHARMACOKINETICS OF LIDOCAINE AND BUPIVACAINE WITH HYALURONIDASE FOR PERIBULBAR BLOCKS.

Authors: N. Nathan, M. Ben Rhaiem, J. Debord, G. Lachatre, P.Feiss.
Affiliation:Dept of Anaesthesiology, Dept of Pharmacology, CHU Dupuytren, 2 Av A Carrel, 87042 Limoges cédex, FRANCE.

Background & goal of the study: Peribulbar anaesthesia with hyaluronidase has gained wide acceptance in ophtalmology because of its lower incidence of complications and its high rate of success. None data are available on the pharmacokinetics of bupivacaine and lidocaine with hyaluronidase during peribulbar blocks. The aim of this study was to evaluate it.

Materials & Methods: Ten patients (mean age: 70.8 ± 3.5 years and weights: 63.0 ± 3.2 kg), scheduled for cataract surgery and intraocular lens implantation were included in the study after ethical committee and patients written informed consents. Peribulbar blocks were achieved percutaneously with plain bupivacaine 0.5 % (5.5 ml), lidocaine 2 % (5.5 ml) and hyaluronidase (80 UI) injected supra and infraorbitally at a maximal distance of 2.5 cm after a negative aspiration check. All patients were premedicated with midazolam 0.1 mg.kg^{-1} IM. Patients were monitored with pulse oxymetry, non invasive blood pressure monitor and EKG. Plasma bupivacaine concentrations were measured by HPLC at regular intervals from the end of injection until the 360th minutes (1). Results are expressed as mean ± SEM.

Results & discussion: Maximum plasma concentrations of lidocaine and bupivacaine were respectively 1.76 ± 0.16 µg.ml^{-1} and 0.45 ± 0.05 µg.ml^{-1} and the corresponding Tmax 7.3 ± 0.9 min and 9.0 ± 1.5 min. Despite a rapid distribution of both anaesthetics, it was not possible to determine classical pharmacokinetic parameters because bioavailabity is not known and because continuous absorption overlap with clearance.

The same Tmax value for the two anaesthetics confirms that other mechanisms than liposolubility participate to the diffusion of local anesthetics from the periocular fat. The Tmax values are far shorter than those obtained during peribulbar block with the same dose of anesthetics without adjunction of hyaluronidase (2). The presence of hyaluronidase more than the type of block which is performed might explain this difference. Indeed, hyaluronidase increases the dispersal of the solution and leads to a more rapid diffusion of the drug. Our Cmax values are far lower than presumed toxic plasma concentrations. Nevertheless at equivalent doses these Cmax are comparable to those observed during endotracheal or paracervical blocks where blood absorption of local anesthetics is very rapid and intense (3).

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A.141

PRELIMINARY IN VIVO EVALUATION OF INTRATHECAL LIPOSOMAL BUPIVACAINE

Dan Benhamou[*], Jean-Marc Malinovsky[#], Franz Legros[$],
Guy Couarraze[*]

Départements d'Anesthésie-Réanimation [*]Université Paris-Sud, Hôpital Antoine Béclère, 92141 Clamart, France
[#]C.H.U., Hôtel-Dieu, 44035 Nantes, France
[$]Laboratory of Physiopathology, Free University of Brussels, Brussels, Belgium

Background-goal of study : There has been intensive research to reduce systemic toxicity associated with the use of the long-acting local anesthetic, bupivacaine. Recently, a novel approach has consisted in encapsulation of bupivacaine into multilamellar liposomes resulting in a reservoir and a slow release of the local anesthetic (1). This work is the first use of liposomal bupivacaine injected intrathecally in rabbits.

Materials and methods : 40 New Zealand white rabbits (3.0 ± 0.3 kg) were included in the study and were fasted the day before the study. A marginal ear vein was cannulated and lactated ringer's solution (20 ml) was infused immediately before intrathecal puncture to provide fluid loading. This vein was also used to administer a sedative dose of thiopental (titrated by 10 mg increments) to avoid any animal movement during the intrathecal puncture. A radiant heat lamp was maintained over the animal to avoid hypothermia. Under local anesthesia and after immobilization of the animal, a femoral artery was cannulated using a 22 g peripheral catheter to provide continuous mean arterial blood pressure (MABP) monitoring and to allow for blood gas sampling (1 ml). In the sedated animal, the intracisternal subarachnoid space was punctured percutaneously through the atlanto-occipital membrane using a 22 g needle while the animal was in a lateral position and had a flexed head. After aspiration of cerebrospinal fluid (CSF), one of the four randomly assigned solution was slowly injected in a volume of 300 µl : group 1 : plain (isobaric) commercial solution of 0.5 % bupivacaine ; group 2 : phosphate buffer saline solution (pH = 8.1) ; group 3 : phosphate buffer saline solution containing empty liposomes ; group 4 : liposomal bupivacaine. Ventilation with air via a face mask was maintained until an efficacious spontaneous ventilation recurs. To maintain MABP above 80 % of its control value, a continuous infusion of dopamine in the ear vein was used (50 mg in 50 ml, 10 to 100 ml/h depending on the severity of the hypotension). MABP was recorded before (control) and 2, 5, 15, 45 et 60 minutes after intrathecal injection. At the same predetermined times, arterial blood was withdrawn. After recovery from the spinal injection, arterial and venous catheters are removed. Duration of motor blockade was evaluated from intrathecal injection to complete motor recovery. Results are expressed as mean ± sd. Statistics included two-way ANOVA and chi-2 analysis. $p < 0.05$ was considered significant.

Results-discussion : Intrathecal injection of phosphate buffer with or without empty liposomes produced no hypotension whereas plain and liposomal bupivacaine decreased significantly MABP during the first 45 minutes after injection. However, requirements for dopamine infusion were significantly lower after liposomal than after plain bupivacaine (47.3 ± 36.2 mg versus 74.3 ± 20.4 mg) Respiratory impairment was longer after plain (14.8 ± 7.6 min) than after liposomal bupivacaine (12.8 ± 7.4 min). Motor blockade lasted longer (126 ± 49 min) after liposomal than after plain (70 ± 23 min) bupivacaine.

Conclusion : Intrathecal liposomal bupivacaine produced less severe hemodynamic and respiratory disturbances but the slow release effect was associated with a prolonged motor blockade.

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A.142

BIODISTRIBUTION OF LIPOSOMAL BUPIVACAINE AFTER EPIDURAL ADMINISTRATION TO RABBITS

Jean G. Boogaerts, MD, PhD, Noëlle D. Lafont, MD,
Franz J. Legros PhD.

Laboratory of Physiopathology, Free University of Brussels,
Campus Erasme, Brussels, Belgium.

Background and goal of study: Liposomes have been tried as drug carriers offering controlled delivery of biologically active agents wich can lead to a prolonged effect and a reduced toxicity(1) . Specifically, local anaesthetics (LA) have been encapsulated into multilamellar (MLV) liposomes with the aim to obtain a longer duration of action or a reduction of circulating plasma levels. Preliminary studies indicated that epidurally injected MLV represent a deposit formulation releasing bupivacaine in a controlled way, ensuring a low, constant and prolonged plasma level (2).The present study compares the plasma levels and the biodistribution of bupivacaine after injection of plain (BP) and encapsulated (BP-MLV) formulations of the LA into the rabbit's epidural space.

Materials and methods: MLV liposomes made of egg phosphadidylcholine and cholesterol in a ratio 4:3, containing 4.5 mg BP and 1μCi ^{3}H-BP in 0.2 ml were injected epidurally at the sacral level to 6 albinos rabbits. An other serie of animals received 4.5 mg of free BP and 1μCi ^{3}H-BP. Plasma arterial levels of BP were determined by counting radioactivity. In each group, rabbits were killed after 2 hours. The BP concentrations in the heart, liver, LCR, and cauda equina were counted after solubilisation on 3 samples of each and expressed in % of the injected dose (%ID). ANOVA and Student's *t* tests.

Results and discussion:

Radioactivity in the whole plasma(%ID) **P<0.01

Time(min)	BP	BP-MLV
15	1.36±0.1	0.0**
30	1.35±0.05	0.10±0.04**
60	1.30±0.05	0.48±0.02**
120	1.0 ±0.1	0.48±0.02**
240		0.47±0.03

Systemic distribution of BP expressed in %ID for the whole organ (liver and heart) or for 1g of tissue (cauda equina) or for 1 ml (LCR). * P<0.05

Tissue	BP	BP-MLV
Liver	20.48±0.49	7.45±1.18**
Heart	2.14±0.49	0.50±0.03**
Cauda equina	0.01±0.00	0.18±0.02**
LCR	0.01±0.00	O**

These results show a low concentration of BP in the heart and liver with the encapsulated form by reduction of vascular resorption of the LA. This raises the hope of a lowered toxicity. Oppositely, the concentration in the cauda equina is more important with BP-MLV than with the free drug. This confirms the slow release of BP from the epidural MLV liposomal depot and explains the prolonged analgesia observed in humans(3).

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A.143

SPINAL CLONIDINE PROLONGS ONSET OF MOTOR BLOCKADE OF BUPIVACAINE

Langenecker S. MD, Kapral S. MD, Taslimi R. MD,
Sauberer A. MD, Chiari A. MD and Weinstabl C. MD.
Department of Anaesthesia and General Intensive Care,
University of Vienna, Vienna, Austria

INTRODUCTION: The addition of clonidine, an α2-adrenoceptor agonist, to local anaesthesia in spinal blockade prolongs blockduration and postoperative analgesia [1]. So far, the onset of sensory and motor blockade was expected not to be influenced by clonidine [2] Aim of our study was to evaluate the effect of clonidine on the initial period of spinal anaesthesia.

PATIENTS AND METHODS: After institutional approval and informed consent was obtained, 24 patients (51 ± 13 yrs, 72 ± 9 kg) scheduled for obstetric surgery were studied. Before spinal puncture 500 ml of Ringer's solution and 5 mg midazolam were administered. Spinal anaesthesia was performed in a sitting position at L4/L5 with a 27 Gauge Whitacre needle. Studydesign: placebo-controlled, double-blind study. Group 1: 3.5 ml of bupivacaine 0.5% and 75 µg Clonidine (Catapresan®, Boehringer Ingelheim, Germany), group 2: 3.5 ml of bupivacaine 0 5% and 0.5 ml NaCl 0.9%. Heart rate (HR), mean arterial pressure (MAP), oxygen saturation (SaO2) and motility of muscles of innervation zone L5 were measured before and in close intervals for 30 minutes after administration of the anaesthetic solution. For quantification of muscle force, we developed a rating scale from 6 (normal motility) to 0 (complete paralysis). Furthermore, time from administration to complete paralysis and to recovery were measured.

RESULTS: In all patients a satisfactory surgical anaesthesia was produced. The onset of motor blockade was significantly delayed in group 1 as compared to the control group 2 (Fig.). Complete paralysis was achieved after 15.3 ± 3.5 min in group 1 and 8.0 ± 5.2 min in group 2 (p<0.05). We found a significant difference in the duration of blockade between the two groups (group1: 8 ± 1.3 hrs, group 2: 4 ± 1.3 hrs; p<0.05). Hemodynamics remained stable in all patients.

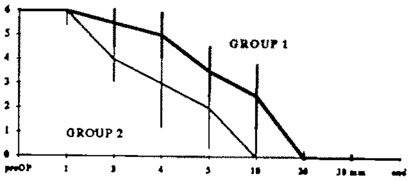

FIGURE ONSET OF MOTOR BLOCKADE

CONCLUSION: We conclude, that spinal clonidine produces not only a pronounced prolongation of duration of blockade, but also a remarkable time-lag of onset of motor blockade.

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A.144

Morbidity following Spinal Anaesthesia in Adolescents

L. Radbruch, J. Lynch, I. Krings-Ernst

Department of Anaesthesiology, University of Cologne and Dreifaltigkeitskrankenhaus, Köln, Germany

Background & goal of study: Reports of increased incidence of postspinal headache are the main reason for the reluctance to use spinal anaesthesia (SA) in younger patients. We evaluated efficacy and complication rates of SA in adolescent patients.

Material & methods: From 1988-92 423 adolescent patients aged 11-21 years (211 female, 212 male) received SA for elective orthopedic in-patient surgery. 224 patients (121 female, 103 male) were less than 18 years old. SA was performed with Whitacre needles in 357 patients and Quincke needles in 66 patients.

Results & discussion: Patient acceptance was high (99%). Needle insertion was rated as difficult in 12% of the patients. General anaesthesia was necessary only in 2 patients because of inadequate SA. Side effects of SA were reported by 16,8% of patients, but were usually mild (postspinal headache (PSH) 5,4%, nausea and vomiting 6,4%, urinary retention 3,6% and back pain 1,4%). Therapeutic interventions were necessary in only 4,5%. 7 Patients with urinary retention were treated with an urinary catheter. In the age group under 18 years side effects were not increased, and the incidence of PSH was 5,3%.

PSH with a duration of 1-6 days was reported by 23 patients. 4 patients received oral analgesic drugs, resulting in pain relief in 3 patients. One patient was pain free after an epidural blood patch.

Table 1:

Needle type	PSH/Patients	
Whitacre 22 gauge	20/322	(6,2%)
Whitacre 25 gauge	0/6	
Whitacre 27 gauge	0/28	
Quincke 25 gauge	2/14	(14,3%)
Quincke 27 gauge	0/20	
Quincke 29 gauge	1/33	(3,0%)

Conclusions: The incidence of postspinal headache as well as other side effects of SA are not increased compared to other studies with older patients[1,2]. Spinal anaesthesia is a safe and efficient procedure for orthopedic surgery in adolescents. The incidence of PSH can be decreased significantly with small diameter Whitacre needles and with fine gauge Quincke tip needles.

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A.145

ULTRASONOGRAPHIC GUIDED STELLATUM GANGLION BLOCKADE

Kapral S. MD*, Gosch M. MD*, Fleischmann D MD#, Kontrus M. MD#, Krafft P. MD* and Weinstabl C. MD*.
*Dept. of Anaesthesia and General Intensive Care, #Dept. of Radiology, University of Vienna, Austria

INTRODUCTION: Stellatum Ganglion Blockade inhibits sympathetic innervation of head, neck and the upper extremity. Positioning of the needle tip at the ganglion bears the risk of injury of adjacent structures. Besides, the successrate of this procedure remains doubtful [1]. The aim of our studie was to develop an ultrasound guided technique for stellatum ganglion blockade.

PATIENTS AND METHODS: In 12 consecutive patients (age: 22-54 yrs, mean age: 42 yrs) with reflex sympathetic dystrophy (n = 3) and after replantation of forearm and hand (n = 9) an ultrasonographic guided (Toshiba SAL 38B with a scanning probe of 10 MHz) stellatum ganglion blockade was performed. After visualisation of the anatomy a 22 G-cannula was introduced towards the transverse process of C6 vertebra. After injection of 5 ml bupivacaine 0.25 % with 1:200.000 epinephrine the spread of the anaesthetic solution was visualised. Cutaneous temperature was documented.

RESULTS: In all patients a Horner's syndrom appeared within the first 10 minutes. There was a significant difference between cutaneous temperature before and 30 minutes after blockade. In all cases the needle tip could be clearly identified near C6. The desired spread of the local anaesthetic solution could be documented in all patients. Side effects could be predicted in 4 of 12 patients (recurrent nerve paresis n=1, blockade of spinal root of C6 n=3).

CONCLUSION: In conclusion, we describe a technique for a safety blockade of the stellatum ganglion using ultrasonographic imaging. This proves to be more reliable and selective than previously described methods.

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A.146

INDIRECT SONOGRAPHIC GUIDANCE FOR EPIDURAL ANAESTHESIA

BONAZZI M.,RIVA A.,LENSI C.,LAVENEZIANA D.,DI GENNARO S.(*)
DEPARTMENT OF ANAESTHESIOLOGY AND RADIOLOGY (*), BASSINI HOSPITAL-MILANO (ITALY)

Background and goal of study: technical difficulties in performing epidural anaesthesia (E A) may result from obesity or edema, which can obscure anatomic landmarks and increase the percutaneous distance between the skin and the epidural space (E S). This study was designed to assess the reliability of sonographic evaluation in the prediction of the depth of E S (1).

Materials and methods: thirty-three patients of both sexes, scheduled for E A were prospectively studied. Patients were placed in a sitting position and sagittal scanning of the lumbar spine was performed with a 5-MHz transducer (Aloka SSD 650) over the fourth or fifth interspace in order to identify the deeper hyperechogen interface, which represents the landmark between ligamentum flavum and E S. Ultrasound depth (U D) was measured and transducer removed. A Tuohy needle 18 G was then introduced percutaneously according with the standard technique and a rubber slide was placed over it, so that its depth of insertion could be measured accurately. The potential for using U D for prediction of distance from skin to E S was analyzed using a simple linear regression analysis; p values < 0.05 were considered significant.

Results: mean values of U S depth and needle depth were respectively 51.7 mm (DS 6.8) and 51.4 mm (DS 6.1), the range was 32-64 mm vs 34-63 mm and the correlation coefficent was 0.94.

Conclusions: U S screening of the lumbar spine provides an accurate measurement of the depth of E S which can facilitate the performance of E A and may decrease the complication rate, particularly in those patients in which anatomic landmarks are obscured. It should prove also a valuable aid in teaching the technique of E A.

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A.147

LOWER LIMB BLOOD FLOW AND LUMBAR PLEXUS BLOCKADE

J.F. Brichant, A.F. Meulders, M. Zicot

Departments of Anesthesiology and Cardiology, Liège University Hospital, CHR de la Citadelle, B-4000 LIEGE

Lower limb blood flow is decreased by general anesthesia while it is increased by epidural anesthesia. This difference might partially explain the decreased rate of deep venous thrombosis observed in patients having undergone lower limb surgery under epidural anesthesia. The present study investigated the effects of lumbar plexus blockade (LPB) by the 3 in 1 technique on lower limb blood flow.

MATERIAL AND METHODS

After patient's informed consent and approval of the study protocol by the Ethics Committee were obtained, 12 ASA 1-2 patients scheduled for lower limb surgery [age (mean ± SD): 77.1 ± 13.5; weight (mean ± SD) : 64.6 ± 19.6] were included in the study. One hour before performance of the LPB, midazolam 5 mg and atropine 0,5 mg were administered intramuscularly along with usual medications. Upon arrival in the anesthesia induction room, patients were equipped with a 3 lead ECG, an automatic non invasive blood pressure device and a peripheral venous line. A first measurement of femoral blood flow was obtained. Thereafter, the LPB was performed by an experienced anesthesiologist using the 3 in 1 technique (1). The femoral nerve was located with a nerve stimulator (Anaestim MK3, MEDA). A current of < 0.5 mA was applied and a 23 gauge insulated Top Pole needle was used. Bupivacaïne (125 mg), clonidine (150 μg) and epinephrine (125 μg) in a 26 ml solution were injected at the femoral nerve. A second femoral blood flow measurement was obtained 30 min after performance of the block. Femoral blood flow was determined in the homolateral (n = 12) and in the controlateral lower limb (n = 8).

Flows in the femoral arteries were measured immediately below the inguinal ligament by a Doppler ultrasound system (Toshiba Sonolayer SSA.100A) combining B mode echo and pulsed Doppler flowmetry. Differences in blood flow rates and sections of the femoral arteries were considered significant for $p < 0.05$ (t-test for paired data).

RESULTS

Lumbar plexus blockade (LPB) was achieved in all patients. Blood flow was similar in both legs at control. LPB increased homolateral femoral blood flow in each patient, whereas controlateral femoral blood flow was not changed. The LPB did not alter heart rate, blood pressure, nor transcutaneous oxymetry.

DISCUSSION

LPB by the 3 in 1 technique induced a significant increase in homolateral lower limb blood. Because this increase was observed in the homolateral and not in the controlateral limb, it is likely related to a local mechanism, e.g. decreased vascular resistance in the area below the block. LPB might be of interest in thromboembolism prophylaxis because reduced blood flow is thought to be responsible of an increased risk of deep vein thrombosis. In addition, it may be safely combined with medications altering coagulation, which is not the case for epidural or spinal anesthesia.

We conclude that LPB induces a significant increase in homolateral lower limb blood flow, making this technique of analgesia potentially interesting in patients with high risk of deep vein thrombosis.

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A.148

Title : WHY POST-OPERATIVE EPIDURAL ANALGESIA IS NOT COMPLETE FOR EVERY PATIENT ?

Authors : FARHAT F, BILLARD V, KUHLMAN G, COUANET D, JAYR C.
Affiliation : Departments of Anesthesiology and Radiology, Institut Gustave-Roussy, Villejuif Cedex, France

Introduction : Epidural infusion of different opioids plus local anesthetic may produce an excellent postoperative analgesia (1). However, analgesia is not complete for every patient. The percentage of patients with unsatisfactory pain relief after epidural analgesia is between 30 and 40 % (1, 2). The aim of this prospective study was : 1. to evaluate the incidence of unsatisfactory pain relief after thoracic epidural analgesia, 2. to find an explanation for this sub-optimal pain relief.

Materials and methods : The study was approved by the local scientific ethical committee and informed consent was obtained from each patient. Patients scheduled for abdominal surgery for cancer were studied. An epidural catheter was placed (T7-T11) before surgery. Bupivacaine 0.5 % (8-10 ml) with epinephrine (1:200.000) and fentanyl (0.1 mg) were injected. Bupivacaine was reinjected until the block attained the T4 level. When this level was obtained general anesthesia was induced with etomidate, atracurium isoflurane, fentanyl (0.1 mg) and O_2/N_2O. Postoperatively, a mixture with bupivacaine 0.125 % (10 ml/h) and morphine (0.25 mg/h) was infused continuously into the epidural space. To quantify the severity of postoperative pain, the patients were asked to use a visual analog scale (VAS : 0-10 cm). The patients scored their pain at rest during the 48 hour postoperative time period. The sensory levels were tested at the same time. In absence of sensory levels, 5 ml of bupivacaine were injected and analgesia levels were tested again. If the score of analgesia was superior to 2 cm at 24 or 48 hours after surgery, a computed-tomography (CT) with contrast medium injection was performed and contrast enhancement of the epidural space was analysed on the CT-scan.

Results : 84 patients were included in the study. 20 patients had suboptimal pain relief (VAS > 2 cm) in the 48 hour postoperative time period. Among these 20 patients, 10 patients did not have any sensory level even after 5 ml bupivacaine (0.5 %) injection, suggesting a complete displacement of the epidural catheter out of the epidural space and therefore CT was not always performed (n = 5). 10 patients had suboptimal pain relief associated with objective sensory level. CT was performed for these 10 patients. For 3 patients, the CT-scan showed a partial removing of the epidural catheter out of the epidural space. For 5 patients, the epidural catheter was well positioned in the epidural space. Finally, for 2 patients the CT-scan showed that the diffusion of the contrast medium was not symetrical in the epidural space.

Conclusion : In this study, epidural analgesia with bupivacaine and opioids provided satisfactory pain relief after abdominal surgery in 76 % of the patients. The suboptimal pain relief was mainly due to a misplacement of the epidural catheter. In only 5 cases, the suboptimal pain relief associated with sensory levels is not explained by a misplacement of the epidural catheter.

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A.149

THE SIZE OF THE DURAL SAC IS UNAFFECTED BY BODY POSITION

J.F. Brichant, V. Magotteaux, J.P. Muller, M. Nizet, P. Hans

Departments of Anesthesiology and Radiology. Liège University Hospital, Citadelle Hospital, B-4000 LIEGE,

Epidural catheter insertion can be performed with the patient in the sitting or in the lateral decubitus position. An advantage of the lateral decubitus position is decreased cerebrospinal fluid pressure at the lumbar level that would reduce the risk of inadvertent dural puncture (1). However, the influence of the patient's position on the size of the dural sac is unknown. Hence, the purpose of the present study was to assess the size of the dural sac in the sitting and in the lateral decubitus position using B mode echography.

METHODS

After approval of the study protocol by the Ethics Committee, 24 healthy volunteers [height (mean ± SD): 170.21 ± 10.49 cm; weight (mean ± SD): 65.88 ± 11.72 kg; age (mean ± SD): 29.08 ± 8.26 years] were studied. Using B Mode echography, we measured at the L2-L3 level the distance between the skin and the posterior face of the dura mater (SDM) and between the skin and the posterior longitudinal ligament (SPLL) both in the sitting and in the lateral decubitus position. During measurements, great care was taken to maintain the ultrasound probe at the same angle to the skin. The ligamentum flavum was not seen because its low echogenicity. In view of the narrowness of the ventral epidural space, we computed the anterior posterior diameter of the dural sac (DSD) as follows : **DSD = SPLL - SDM.** SPLL and SDM in the lateral decubitus and in the sitting position were compared using a Student's t test for paired data. In addition, linear regression analysis was used to test for correlations between DSD, SPLL, SDM and Body Mass Index (BMI).

RESULTS

The size of the dural sac (DSD), the distance between the skin and the posterior longitudinal ligament (SPLL) or between the skin and the dura mater (SDM) were not changed by the patient's body position (table). The Body Mass Index (BMI) was correlated with SPLL ($r = 0.47$) ($p < 0.001$) and SDM ($r = 0.62$)($p < 0.001$). No significant correlation was found between DSD, weight, height or BMI.

TABLE (mean ± SD)	SPLL (mm)	SDM (mm)	DSD (mm)
Sitting	55.8 ± 4.6	45.9 ± 4.7	9.9 ± 1.1
Lat. decub.	55.4 ± 5.0	45.7 ± 5.2	9.8 ± 1.0

DISCUSSION

Our results indicate that the diameter of the dural sac is not altered by the patient's position, suggesting that epidural space size is unchanged. Indeed, any change in the size of the dural sac should result in a change of the posterior epidural space size since these are the two main structures on the midline of the vertebral canal, an unexpandable bony structure.

Our study reveals also that SDM and SPLL are correlated with BMI as is the distance between the skin and the epidural space (2). We failed to find any correlation between the diameter of the dural sac and weight, height or BMI. This is consistant with a previous study that failed to find any correlation between epidural space size and any of these parameters (3).

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A.150

FREQUENCY OF A TRAIN-OF-FOUR ULNAR NERVE STIMULATION INFLUENCES NEUROMUSCULAR RESPONSE

Olli A Meretoja, Tomi Taivainen,
Barbara W Brandom, Kari Wirtavuori

Departments of Anaesthesiology, Children's Hospital
University of Helsinki, Helsinki, Finland, and
Children's Hospital of Pittsburgh, Pittsburgh, USA

Background and goal of study: Neuromuscular block (NMB) is commonly assessed by using either a single twitch or a train-of-four (TOF) ulnar nerve stimulation. A single twitch stimulation produces greater NMB if used at 1-4 sec intervals instead of a 7-10 sec interval [1]. Furthermore, a TOF stimulation produces greater NMB than a single twitch stimulation at same frequency [2]. As two frequencies of TOF stimuli have not been compared, we assessed onset and depth of NMB when a TOF stimulation (2 Hz) of ulnar nerve was used once every 10 or 20 sec.

Patients and methods: With ethics committee approval and informed consent, 24 (ASA 1-2) children of 2-12 years of age were studied. After midazolam premedication, anaesthesia was induced and maintained by propofol, alfentanil and N_2O-O_2. Adductor pollicis EMG was recorded in both hands which were randomized for stimulation frequency. Each patient received one dose of atracurium 140, vecuronium 40 or mivacurium 70 µg/kg. Maximal NMB and onset time (time from administration to maximal effect) were compared by ANOVA or paired *t*-test. P-value of <0.05 was significant. Data are mean ± SEM.

Results: Palmar skin temperatures were >33°C. Onset times were shorter for the faster stimulation pattern (Δ onset time was 21 ± 10 sec, P < 0.05). Maximal NMB did not differ between muscle relaxants, but was greater for the faster stimulation pattern (74 ± 5% *vs.* 52 ± 4% NMB, P = 0.0001) (table).

Table. NMB following atracurium, vecuronium or mivacurium

	Atracurium	Vecuronium	Mivacurium
Onset time (min)			
TOF every 10 sec	4.8 ± 0.3	4.0 ± 0.2	2.6 ± 0.2
TOF every 20 sec	5.4 ± 0.2	4.2 ± 0.3	2.8 ± 0.3
Maximal NMB (%)			
TOF every 10 sec	69.6 ± 7.7	80.8 ± 6.1	73.0 ± 9.9
TOF every 20 sec	53.8 ± 5.9	59.8 ± 6.0	42.5 ± 5.9

Conclusion: Even a common difference in the frequency of a TOF stimulation (every 10 or 20 sec) significantly influences potency estimates of muscle relaxants. This factor should be constant when the potency of muscle relaxants is tested.

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A.151

ONSET TIME AND INTUBATION CHARACTERISTICS OF MIVACURIUM

Jean-Claude De Mey, Georges Rolly

Department of Anaesthesia,
University of Ghent, Belgium

Background and goal of study : Mivacurium (MIV) is a potent, shortacting non depolarizing relaxant. This study evaluates onset and depth of neuromuscular blockade, intubation conditions and haemodynamic changes after an intubation dose of 0.15 mg/kg (± $2xED_{95}$).

Materials and methods : After approval of the Ethics Committee, 60 informed ASA I or II patients were included in the study. Premedication consisted of diazepam 10 mg orally, and anaesthesia was done with alfentanil 15 µg/kg (followed by 60 µg/kg/h) and propofol 2 mg/kg (followed by 9 mg/kg/h for 20 min. and later on 6 mg/kg/h). After supramaximal stimulus registration (Datex Relaxograph) MIV 0.15 mg/kg was given and intubation attempted once T_1 decreased below 25 %. Time to 25, 50, 75 and 90 % block, to successful intubation with corresponding % of block and intubating conditions were assessed, as well as max. block and time to it.

Results and discussion : Mean ± SD values of age, weight and height were respectively 40.9 ± 14.4 y, 68.4 ± 11.2 kg and 169.7 + 9.2 cm. The times from injection to different % blocks are as follows : 25 % (85 ± 35 sec), 50 % (112 ± 41), 75 % (156 ± 55) and 90 % (224 ± 97). The max. block was 92 % (range 43-100). Intubation was possible 192 ± 122 sec. after injection at 79.0 ± 2.9 % of block and reported as excellent in 41 (68 %), as good in 15 (25 %), as poor in 3 (5 %) and bad in 1 (2 %) of the patients. In all but 4 patients intubation was possible after a single dose of 0.15 mg/kg. All but 1 patients could be intubated at the first attempt. Syst. and diast. BP decreased (p>0.001) 1 min after MIV and heart rate decreased significantly 1 and 5 min. after MIV.

Conclusion : MIV, in a dose of 0.15 mg/kg, is not a valuable alternative for succinylcholine. Using higher doses or a priming dose might create faster optimal intubation conditions and approach the profile of a non depolarizing succinylcholine.

A.152

COMPARATIVE EFFECTS OF ATRACURIUM AND VECURONIUM ON INTRAOCULAR PRESSURE

H. Polarz, H. Böhrer, W. v. Tabouillot, B. Pfau, E. Martin

Depts. of Anaesthesia and Ophthalmology, Univ. of Heidelberg, D-69120 Heidelberg, Germany

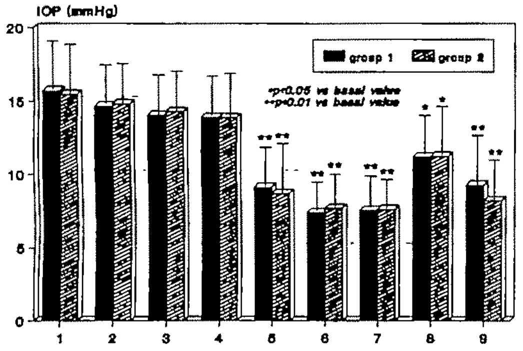
Introduction: Depolarizing muscle relaxants are known to increase intraocular pressure (1). Atracurium and vecuronium have been found to exert variable effects on intraocular pressure (2, 3). Aim of our study was to assess the influence of atracurium and vecuronium on intraocular pressure (IOP) under clinical conditions.

Methods: With institutional approval and informed consent, 40 ASA II or III patients undergoing ophthalmic surgery were studied. Following oral premedication with dipotassium clorazepate 0.3 mg/kg, anaesthesia was induced with thiopentone 3-4 mg/kg and alfentanil 15 µg/kg. Muscle relaxation was provided according to randomization. Group 1 patients received atracurium 0.3 mg/kg. Patients in group 2 were given vecuronium 0.07 mg/kg. Anaesthesia was maintained with isoflurane 0.5-0.8 vol% and 70% nitrous oxide in oxygen. The trachea was intubated 4 minutes after induction and muscle relaxation.

All measurements of IOP were performed on the eye not scheduled for surgery. IOP was measured in the supine position using a Möller-Wedel applanation tonometer. Values were recorded in the morning of the operating day prior to premedication (1), 30 (2) and 45 minutes (3) after premedication, prior to induction of anaesthesia (4), 1 (5), 2, (6) and 3 (7) minutes after induction of anaesthesia and muscle relaxation, and immediately after (8) and 5 minutes after (9) endotracheal intubation.

The results are presented as mean ± SD. Data were analyzed by analysis of variance and *t* tests with Bonferroni corrections.

Results:



Discussion: In both groups, there was a significant decrease in IOP after induction of anesthesia with thiopentone, alfentanil, and atracurium or vecuronium (fig.). No differences in IOP were found between groups. Thus, both muscle relaxants can be administered when increases in IOP have to be avoided.

References:

1. Cook JH: Anaesthesia 1981; 36: 359-65.
2. Schneider HJ, et al: Anesth Analg 1986; 65: 877-82.
3. Lavery GG, et al· Can Anaesth Soc J 1986; 33: 437-42.

A.153

RESIDUAL CURARISATION FOLLOWING VECURONIUM OR ATRACURIUM BY BOLUS OR INFUSION.

WJ Fawcett and JN Cashman.

Department of Anaesthetics, St. George's Hospital and Medical School, London, England.

Background. Postoperative Residual Curarisation (PORC) occurs in up to 20-48% of patients following the use of pancuronium and curare (1,2), and up to 9% following atracurium and vecuronium (3). For longer surgical procedures, some advocate the use of atracurium and vecuronium by infusion, although there is no data on the incidence of PORC following this technique. The aim of this study was to compare the incidence of PORC following bolus dosing and that following infusion of either atracurium or vecuronium.

Methods. The protocol was approved by the local ethics committee. One hundred and fifty patients (100 in the bolus group, 50 in the infusion group) were studied following a range of surgical procedures with the anaesthetist unaware that the patient was to be assessed postoperatively. On arrival in the recovery room compound evoked EMG's were measured in response to a train of four (TOF) pattern with recording electrodes over the hypothenar eminence (Datex Relaxograph). Adequate neuromuscular reversal was assessed clinically by the ability to maintain a head lift >5 secs. The total dose of neuromuscular blocking agent used, duration of anaesthesia, dose and timing of the reversal agent, and any other factors likely to affect the duration of neuromuscular blockade were also noted. PORC was defined as a TOF ratio of <0.7.

Results and Discussion. The incidence of PORC on arrival in the recovery room was 12% in the bolus group, compared to 24% in the infusion group. Clincal grading of recovery yielded different results, with 47% of patients in the bolus group, and 66% of patients in the infusion group unable to maintain headlift >5 seconds. In the bolus group, however, the duration of anaesthesia was longer, with a median time of 182 cf 70 minutes ($P < 0.01$), and the patients were older (median age 57 vs 44 years - $P < 0.05$). The rate of infusion of drugs in the two groups was not significantly different, with a median dose of 2.06 ED_{95}/kg/hr in the infusion group and 1.87 in the bolus group. The use of a peripheral nerve stimulator was not associated with a lower incidence of PORC in either group. No patient exhibited signs of respiratory difficulty. Thus, our results for bolus dosing are in agreement with other workers, whereasthe incidence of PORC, following infusion of these agents approaches that seen when pancuronium and curare are used.

References:

1. Andersen BN et al. Acta Anaesthesiol Scand. 1988; 32: 79-81.
2. Brull SJ et al. Can J. Anaesth. 1991; 38: 164-8.
3. Bevan DR et al. Anesthesiology. 1988; 69: 272-276.

A.154

DOSE REQUIREMENTS, REVERSIBILITY AND PHARMACOKINETICS OF ORG 9487.

J.M.K.H. Wierda, MD PhD, L. van den Broek, MD, N.J. Smeulers, MD.

Research Group for Experimental Anesthesiology and Clinical Pharmacology, University Hospital Groningen, P.O.Box 30.001, 9700 RB Groningen, the Netherlands.

INTRODUCTION: A bolus dose of Org 9487, a new steroidal non-depolarizing muscle relaxant with fast onset and short duration, has been shown to be a serious alternative for succinylcholine when short-lasting relaxation is required [1]. We studied the dose requirement, reversibility and pharmacokinetics of Org 9487 using a bolus dose followed by an infusion.

METHODS: After approval by the medical ethics committee and informed consent, ten patients classified as ASA I or II were studied. After induction with fentanyl, 1-3 $\mu g.kg^{-1}$, and propofol, 1.5-2.5 $mg.kg^{-1}$, anaesthesia was maintained with isoflurane, 1% inspiratory concentration, added to a mixture of O_2 and N_2O (1:2). At 0 min patients received an intubating dose of Org 9487, 1.5 $mg.kg^{-1}$ (1.3x ED_{90}). At 5% recovery of the twitch height an infusion of Org 9487, 5 $mg.kg^{-1}.hr^{-1}$, was started. The rate was adjusted to maintain the neuromuscular block between 80 and 90%. During infusion of Org 9487 five patients received neostigmine, 40 $\mu g.kg^{-1}$, and methyl-atropine, 7 $\mu g.kg^{-1}$ at 50 min. The infusion of Org 9487 was stopped at 60 min. Neuromuscular block was monitored mechanomyographically with single twitch (0.1 Hz). Recovery and reversal were also quantified by measuring the percentage train-of-four (TOF) at intervals. Plasma concentrations of Org 9487 and its putative metabolites were measured by chromatography (HPLC) and the pharmacokinetic variables calculated using iterative linear least square regression analysis (MULTIFIT®). Pharmacodynamic and pharmacokinetic data are presented as Mean(CV).

RESULTS: Infusion started at 8(21) min after the bolus dose; thereafter maintenance dose requirement of Org 9487 was 3.36(29) $mg.kg^{-1}.hr^{-1}$, resulting in an average neuromuscular block of 83(4)%. At 50 min following bolus administration, just before neostigmine, twitch height was 15.4(12)% and TOF was 1.4(221)%; 10 min after neostigmine twitch height was 81(30)% and TOF was 38(21)%. After stopping the infusion at 60 min a $TOF_{70\%}$ was reached at 74.5(8) min in the patients who received neostigmine. In the five patients who did not receive neostigmine a $TOF_{70\%}$ was obtained at 97.9(13) min. A biexponential equation adequately described the course of the Org 9487 plasma concentrations. The $t_{½\alpha}$ and $t_{½\beta}$ were 6.3(29) and 71.7(34) min, respectively. Vd_{ss} was 0.29(54) $L.kg^{-1}$. CL_{pl} was 8.5(30) $ml.kg^{-1}.min^{-1}$.

CONCLUSION: Org 9487 is suitable for infusion since the degree of block is easily adjustable. The recovery after one hour infusion is somewhat longer than after a bolus dose [1]. An Org 9487-maintained neuromuscular block, however, is readily reversible by neostigmine.

REFERENCE: 1. Anesthesiology 1992;77:A970.

A.155

EVALUATION OF THE EFFECTS OF ROCURONIUM BROMIDE (ROCURONIUM 9426) ON HAEMODYNAMICS AND LEFT VENTRICULAR FUNCTION IN PATIENTS UNDERGOING ABDOMINAL AORTIC SURGERY

C. Gomez, J.P. Cornet, M.L. Gosgnach, P. Coriat, P. Viars
Département d'Anesthésie-Réanimation, G.H. Pitié-Salpêtrière, 75013 Paris, France

Pancuronium has been shown to provoke myocardial ischemia by increasing heart rate, in patients undergoing coronary artery surgery under high dose fentanyl anaesthesia (1). Mivacurium and atracurium are mild histaminic releasers, which may decrease blood pressure

The aim of this study is to determine left ventricular function response to the administration of rocuronium, a new non depolarising neuromuscular blocking agent.

Methods : 16 patients undergoing aortic surgery were studied. Following induction of anaesthesia with iv fentanyl and flunitrazepam, tracheal intubation was facilitated by local anaesthetic spray. A transoesophageal echocardiography (TEE) probe was inserted after induction. Hemodynamic and TEE measurements were then performed in a steady-state while under mechanical ventilation (Baseline). Thereafter, patients received the muscle relaxant as a simple bolus at two different doses : 0,6 mg/kg in the first 8 pts and 0,9 mg/kg in the following. Measurement were repeated 2 min, 5 min and 10 min after rocuronium injection.

Myocardial ischemia was detected from both ST segment (computerised analysis) and regional left ventricular function changes.

Results : No ischemic episode was detected. As shown in the table hemodynamic and echocardiographic parameters remained stable throughout the study period (table 1 : results in 16 pts)

x ± SD	**after induction**	**+ 2**	**+ 5**	**+ 10 min**
MAP	62	68	70	71
mmHg	± 2	± 2	± 2	± 2
HR	56	59	59	58
b.min	± 3	± 3	± 3	± 3
CI	2,2	2,2	2,2	2,2
$l/min/m^2$	± 0,3	± 0,3	± 0,3	0,4
EFa	50	50	50	50
%	± 3	± 3	± 3	± 3

Discussion : These results demonstrate that hemodynamics, LV function and myocardial oxygenation are not affected by rocuronium when given in combination with low dose fentanyl and benzodiazepine in high risk patients undergoing non cardiac surgery.

(1) Thomson IR : Anesthesiology 62, 708, 1985

A.156

SEDATIVE AND ANXIOLYTIC INTERACTIONS OF CLONIDINE AND BENZODIAZEPINES

P.J.Kulka, M.Tryba, C.Lang, V.Kolhorst , V.Vogt

Department of Anaesthesiology, Intensive Care- and Pain Therapy
University Hospital 'Bergmannsheil' Bochum, FRG

Introduction: Recently clonidine has been investigated for premedication. We evaluated the influence of clonidine alone or in combination with flunitrazepam on preoperative anxiety and sedation as data on this topic are conflicting (1, 2).

Method: After approval by the local ethical committee 160 patients were randomly assigned to receive flunitrazepam 2 mg (F2), flunitrazepam 1 mg + 150 µg clonidine (F1/C150) flunitrazepam 1 mg + 300 µg clonidine (F1/C300) or clonidine 300 µg (C300) orally. Anxiety was assessed by the State Trate Anxiety Inventory (STAI) (3) and a visual-analog scale (VAS) (self assessment) the evening prior to operation (A) and 1 hour after premedication (B). An investigator scored sedation 1 hour after premedication (VAS). Patients were closely monitored after premedication. For statistical evaluation t-test was performed (P<0.05).

Results: After F1/C150 and F1/C300 anxiolysis and sedation increased similarly compared with F2. Sedation and anxiolysis after C300 was inferior to F2. No side effects limiting the use of any of the premedication regimen used in this study were observed.

	F2	F1/C150	F1/C300	C300
STAI A	44 ±12	40 ±8.1	40 ±10.8	41 ±9.7
STAI B	34 ±8.1	32 ±8.1	30 ±8.8	36 ±10.5 a, c
VAS A anxiety	36 ±26	29 ±21	28 ±20	30 ±26
VAS B anxiety	21 ±17	19 ±20	12 ±16	23 ±25 c
VAS sedation	4.9 ±2.2	5.5 ±2.6 d	6.3 ±2 a, d	3.9 ±2.1 a

a: P<0.05 vs. F2; **c**: P<0.05 vs. F1/C300; **d**: P<0.05 vs. C300

Conclusion: According to sedative and axiolytic effects F1/C150 was equivalent to F2. Increasing the clonidine dose increased the sedative and anxiolytic effect while clonidine alone was less effective.

References: 1.Pouttu J, et al: Oral premedication with clonidine: effects on stress response during general surgery. Acta Anaesth Scand 1987; 31: 730-734.

2. Carabine UA, et al: Preanaesthetic medication with clonidine: a dose response study. Br J Anaesth 1991; 67: 79-83.

3. Spielberger CD, et al: Emotional reactions to surgery. J Consult Clin Psych 1973; 40: 33-38.

A.157

PREMEDICATION WITH DEXMEDETOMIDINE A NOVEL α_2-ADRENOCEPTOR AGONIST: SEDATIVE AND ANXIOLYTIC EFFECTS

M. Tryba, A. Schulte-Tamburen, P.J. Kulka, M. Zenz

Department of Anaesthesiology, Intensive Care Medicine and Pain Therapy, University Hospital Bergmannsheil Bochum, Germany

Introduction: Several beneficial effects have been demonstrated for clonidine in anaesthetic use. The putative sedative and anxiolytic properties of α2-adrenoceptor agonists could also be valuable in this context. Dexmedetomidine (Dex) is a novel, more potent and selective α2-adrenoceptor agonist compared to clonidine.

Methods: After approval of the local ethical committee60 healthy male ASA I - II patients were randomly assigned to receive placebo or 2.5 µg / kg Dex intramuscularly about 30 - 45 min prior to induction of anaesthesia for premedication. Values for subjective anxiety and sedation were obtained by means of 100 mm horizontal Visual Analog Scales immediately before premedication and five minutes before induction of anaesthesia
(Sedation: VAS 0 = fully allert - VAS100 = almost asleep;
Anxiety: VAS 0 = calm - VAS100 = panicky).
Statistical analysis of the data were performed with ANOVA with $p < 0.05$.

Results: Demographic data and baseline parameters were similar in both groups (Table). Sedation increased significantlyin the Dex group only (Table). No anxiolytic effects could be ob-served in any of the groups.

	Placebo	Dexmedetomidine
Age (y.)	28.9 ± 6.8	30.4 ± 6.9
B.W. (kg)	81.1 ± 13.2	79.9 ± 9.3
Height (cm)	181.2 ± 8.8	179.9 ± 6.2
ASA I / II	30 / 0	28 / 2
Sedation pre	23.5 ± 18.5	21.9 ± 15.2
post	30.3 ± 22.5	54.7 ± 30.7 *
Anxiety pre	19.3 ± 16.6	31.5 ± 28.7
post	23.2 ± 24.9	30.1 ± 26.6

*** $p < 0.05$**

Conclusion: 2.5 µg / kg Dex i.m. 30 min before induction of anaesthesia produced significant sedation. However, due to the lack of anxiolysis α2-adrenoceptor-agonists may not be optimal as the sole drug for premedication.

A.158

INTRAOPERATIVE REQUIREMENTS OF ISOFLURANE AFTER THE ADMINISTRATION OF INTRAMUSCULAR OR EPIDURAL CLONIDINE

J. Vallès, E. Samsó, X. Vilar, M.M. Puig
Department of Anaesthesiology, IMIM, Hospital Universitario del Mar, Barcelona, Spain.

Alpha-2 adrenergic agonists decrease intra and post-op analgesic requirements when administered transdermal, p.o., i.v., i.m., or epidural. In a recent communication we have established that epidural (EP) administration of clonidine decreases the anaesthetic requirements of fentanyl and isoflurane during epi-general anaesthesia⁽¹⁾. The aim of the present study is to compare the effects of 300 μg of EP or IM clonidine, on isoflurane anaesthetic requirements and post-operative analgesia.

Materials and Methods: Thirty ASA I-II patients scheduled for total hysterectomy were randomly distributed in a double blind manner, into three groups:

Group I	(Clonidine EP.	+ Saline i.m.)
Group II	(Saline EP	+ Clonidine i.m.)
Group III	(Saline EP.	+ Saline i.m.).

EP and IM treatments were administered in a volume of 15 and 2 mL respectively; clonidine was given at a dose of 300 μg both EP and IM. After placement of an EP catheter, all patients received EP and IM injections according to the mentioned groups. At this time, general anaesthesia was induced with atropine, midazolam, thiopental, and vecuronium. Surgical anaesthesia was maintained with 60% N2O in O2 plus isoflurane (IS) administered at the concentrations required to keep mean blood pressure (MBP) and heart rate (HR) within 20% of baseline values. Results are expressed in % expired IS (weighted mean of overall concentrations obtained by mass spectrometry) and time (min) of analgesic request

Results and discussion : All groups were similar in respect to age, Body Mass Index, MBP, HR, and duration of surgery. Intraoperative IS requirements and time of post-op analgesia request (AR) are shown in the table:

GROUP	% IS	AR (min)
I	0.147±0.026 *	120±4 **
II	0.135±0.040 *	27±4
III	0.452±0.131	36±6

Mean±SEM *P<0.05 and **p<0.01

Our results demonstrate that the isoflurane sparing effects of clonidine are similar after EP or IM administration. However, time of AR was signifficantly greater after EP clonidine. These results suggest that the intraoperative analgesic/sedative effects of clonidine could be mediated by alpha-2 adrenergic receptors located mainly at supraspinal sites. In addition, the the differences in AR time between groups I and II indicates that the post-op analgesic effect could be mediated by alpha-2 receptors localted at spinal sites.

References: (1) Samsó et al, Brit J Anaes, 1993;70,S1

A.159

TITLE: EVALUATION OF THE ANTIEMETIC PROPERTIES OF DOLASETRON MESILATE IN GYNECOLOGICAL SURGERY

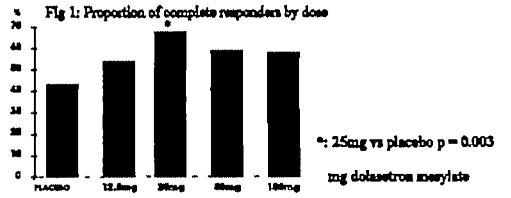
AUTHORS: P. Diemunsch, M.D.*, S. Navé, M.D.+, L.J. Meyerson, Ph.D.+
AFFILIATION: *Hôpitaux Universitaires, D.A.R.; and +Marion Merrell Dow, Clinical Research, F-67000 Strasbourg.

Dolasetron mesilate (Dol), a new 5-HT3 receptor antagonist has been shown to prevent chemotherapy-induced emesis[1,2]. The purpose of this multicenter study was to establish the efficacy and appropriate dose of Dol as an antiemetic agent after surgery under general anesthesia.

Methods: After institutional approval, 281 ASA I/II consenting patients scheduled for inpatient gynecological surgery were enrolled. Study population was stratified into 2 groups: laparoscopic (A) and non-laparoscopic (B) major surgery. After premedication with oral diazepam 5-10 mg, general endotracheal anesthesia consisted of thiopental, fentanyl (F) and vecuronium (V) or succinylcholine for induction, and N_2O in O_2 with isoflurane plus F and V as needed for maintenance. Reversal with neostigmine and atropine was optional. At cessation of anesthesia (To), patients received in a double-blind, randomized fashion over 5 minutes an IV infusion of 50 ml normal saline containing either Dol 12.5, 25, 50, 100 mg or placebo (Pla). The occurrence of emetic episodes, administration of escape antiemetic therapy and adverse reactions were checked every hour for a 24-hour period beginning at To. Antiemetic efficacy was defined as the absence of any emetic episode (i.e. complete response) and escape medication during the 24-h study period. Complete response rates were compared between study groups using logistic regression and contrast between 25 mg and Pla.

Results: There was no significant imbalance in demographic data among the 5 treatment groups (Pla; Dol 12.5mg; Dol 25mg; Dol 50mg; Dol 100 mg). As there were no differences between group A and B for the proportion of complete responders by dose, stratification according to type of surgery was not taken into account and results are given with the 281 patients (of which 4 were in violation of protocol) considered as a single group (Fig. 1).

Fig 1: Proportion of complete responders by dose



No significant side-effects were attributed to dolasetron.

Discussion: Dolasetron 25 mg appears to be effective in preventing post-operative emesis in gynecological surgery under general anesthesia. Our data suggest that no additional benefit would be obtained with the higher dosages. However, further studies are needed to confirm these early results.

1. Proc. ASCO 1992,11:1325.
2. Proc. ASCO 1992,11:1377.

* On behalf of the European Dolasetron group.
Study supported by Marion Merrell Dow.

A.160

TITLE: NO ACUTE TOLERANCE TO ALFENTANIL DURING ANAESTHESIA.

Authors: H.J.M. Lemmens, MD, PhD, C.J.G.M. Jacobs, MD, J.G. Bovill, MD, PhD, A.G.L. Burm, PhD.
Affiliation: Dept. of Anesthesiology, University Hospital, P.O. Box 9600, 2300 RC Leiden, The Netherlands.

The role of acute tolerance to opioids during anaesthesia is unclear. We studied the possible development of acute tolerance to alfentanil during prolonged alfentanil-N_2O anaesthesia in surgical patients.

Methods: With institutional approval and informed consent 20 females, ASA 1, aged 30 - 58 yrs, undergoing prolonged surgery were studied. Anaesthesia was induced with 66% N_2O in O_2 and alfentanil by a computer controlled infusion pump to a target plasma concentration of 700 ng/ml (Cp95 for intubation). Arterial blood pressure and heart rate were continuously measured. Succinylcholine 1 mg/kg was given, and the trachea was intubated 4 min after the target alfentanil plasma concentration had been reached. Thereafter, the alfentanil concentration was reduced by 50 ng/ml and laryngoscopy was performed 4 min after reaching the new target concentration. This procedure was repeated until a haemodynamic response, i.e. an increase in heart rate or systolic blood pressure > 20%, to laryngoscopy occurred. Laryngoscopies were performed by the same person using a laryngoscope with a built in transducer to measure force. Force was exerted in the direction of the handle and maintained at 25 N for 10 sec. During surgery alfentanil was administered by the computer controlled infusion pump and the alfentanil plasma concentration was continuously predicted. At the end of surgery a target alfentanil concentration of 700 ng/ml was obtained and a procedure identical to that before the start of surgery, was performed until a haemodynamic response to laryngoscopy occurred. Arterial blood samples for the determination of the total and unbound alfentanil plasma concentrations were taken before each laryngoscopy. A one tailed paired t-test was used to compare the total and free alfentanil plasma concentrations associated with a response to laryngoscopy before and after surgery.

Results: Anaesthesia time was 214 ± 58 min. The total alfentanil plasma concentrations associated with a haemodynamic response to laryngoscopy before and after surgery were 445 ± 226 ng/ml and 371 ± 145 ng/ml, and the free (unbound) alfentanil plasma concentrations were 43.5 ± 38.7 ng/ml and 36.9 ± 21.8 ng/ml, respectively.

Conclusion: Neither total nor free alfentanil plasma concentrations associated with a haemodynamic response to laryngoscopy were higher at the end of surgery. No evidence for the development of acute tolerance to alfentanil could be demonstrated.

A.161

Pharmacokinetics of intranasal alfentanil

Hans Walter Striebel, Rolf Schwagmeier,
Natalie Boerger, Andreas Tritsch

Department of Anaesthesiology and Intensive Care Medicine
Steglitz Medical Center, Free University of Berlin

Backgroung and goal of the study: During the last few years there has been an increased search for alternative, non invasive methods of opioid administration. Due to its rapid onset of action, the intranasal mode of opioid administration is suitable for demand-adapted titration (1, 2). To date there is a lack of pharmacokinetic data regarding intranasal alfentanil. In this prospective, randomized and double-blind cross-over study, the intranasal as well as intravenous administration of alfentanil was investigated in volunteers.

Materials and methods: Ten volunteers received at random either 12 sprays (0.54 mg) of alfentanil intranasally and simultaneously 12 ml of NaCl 0.9 % intravenously (i.n. group) or 12 sprays of NaCl 0.9 % intranasally and 12 ml of a diluted alfentanil solution (0.54 mg) intravenously (i.v. group). Venous blood was sampled from a cubital vein 3, 6, 9, 12, 15, 20, 30, 60 and 120 minutes after administration. Each subject was assigned once to the i.n. and once to the i.v. group.

Results and discussion: The pharmacokinetic data obtained are presented in Table 1 (mean ± SD). No subject complained about pain or burning intranasally following alfentanil or placebo administration.

	i.v. group		i.n. group		
C_{max}	39.7	±11.9	20.1	± 7.3	ng/ml
t_{max}	3.0	±0	9.0	± 2.1	min
AUC $_{t0-t\infty}$	1958.5	±905.4	1279	± 591.2	min*ng/ml
clearance	315.3	±103.8	519.5	± 278	ml/min
bioavailibility $_{i.n}$			64.75 ± 23.9 %		

Table 1: Pharmacokinetic data obtained from the i.v. and the i.n. group

Conclusion: This pharmacokinetic study demonstrates a rapid rise in plasma concentrations following intranasal administration of alfentanil as well as a high bioavailability.

References: 1.) Striebel HW, et al: Postoperative pain management by intranasal demand-adapted Fentanyl titration. Anesthesiology 1992; 77:281-285
2.) Striebel HW, et al: Intranasal meperidine titration for postoperative pain relief. Anesth Analg 1993; 76: 1047-1051

A.162

Effect of haemodynamics on the first-pass retention of alfentanil in pigs.

F. Boer, J.G. Bovill, A.G.L. Burm and A. Hak.
Dept. of Anaesthesiology, University Hospital, Leiden, The Netherlands.

Background & goal: Alfentanil (A) undergoes moderate first-pass retention in the lungs [1]. If a pulmonary retention is flow-limited then one would expect that changes in total or regional pulmonary blood flow would alter A pulmonary retention. We have studied the effect of major haemodynamic changes on the first-pass pulmonary retention of alfentanil in pigs.

Materials & methods: 6 landrace pigs, 34.7 (1.2) kg, premedicated with ketamine 20 mg/kg, were studied during anaesthesia with isoflurane 0.6-1% and 66% N_2O nitrous oxide in air. Pancuronium 6 mg was given for muscle relaxation. The lungs were ventilated with IPPV and the end-tidal CO_2 was maintained between 4.5-5% vol. Catheters were placed via the right internal jugular vein into the right atrium and, after sternotomy, in the root of the aortic arch. Pulmonary uptake was studied during three 10-min periods, separated by two 14 min resting periods in which haemodynamic parameters were allowed to return to control values. In the beginning of each 10-min period the haemodynamic condition was created and at the end of the period the first-pass uptake of alfentanil was evaluated. The haemodynamic conditions were control, partial inferior vena cava clamping (IVC) and complete right pulmonary artery (RPA) clamping, the order of which was randomised. The first-pass retention of A was studied using a double-indicator dilution technique. A 80 μg mixed with indocyanine green (ICG) 8.6 mg was injected in 1-2 s via the right arterial catheter. Using a fraction collector blood samples from the aorta were taken at 2 s intervals for 120 s after drug injection. In each sample ICG and A concentrations were measured. From the dose-corrected ICG and A concentrations curves cardiac output (C.O.), pulmonary blood volume (P.B.V.), peak extraction (E_p) and first pass retention ($R_{1st-pass}$) were calculated, using standard formulae. Data were analysed with ANOVA, followed by a Newman Keuls test when indicated. Values are mean (SD).

Results & discussion:

	Control	IVC	RPA
C.O. ($l\ min^{-1}$)	2.19 (0.33)	0.91 (0.15)*	1.65 (0.64)
P.B.V. (L)	0.44 (0.06)	0.24 (0.06)*	0.31 (0.08)
E_p (%)	58.6 (10.8)	74.6 (11.3)*	53.9 (6.3)
$R_{1st-pass}$ (%)	26.9 (9.7)	31.0 (17.8)	20.3 (14.4)

* $P<0.05$

Despite marked haemodynamic changes during clamping of IVC or RPA, the first-pass retention of A did not change.

Conclusion: We conclude that A pulmonary first-pass retention is not flow-limited, at least within the flows encountered in this study.

Reference: 1. Boer F. et al. Uptake of sufentanil, alfentanil and morphine in the lungs of patients about to undergo coronary artery surgery. Br J Anaesth 1992; 68: 370-375.

A.163

FIRST PASS PULMONARY UPTAKE OF THEOPHYLLINE IN VENTILATED PATIENTS.

P. Jambou*, M.D., J. Levraut*, M.D., D. Jambou **, M.D-PhD, J. Giudicelli *** PhD, Ph. Lapalus **, M.D-PhD, D. Grimaud*, M.D. (*Anes Dept., **Pharmacol. Dept., ***Biochem Dept., CHU Nice, FRANCE)

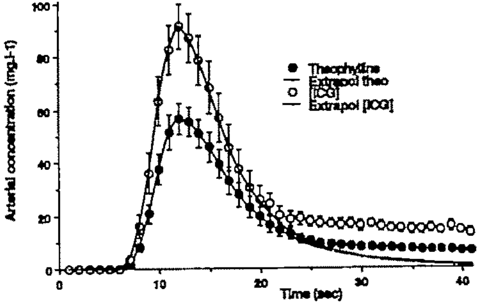
Background and goal of the study : After intravenous injection (IV), many drugs exhibit a high pulmonary first-pass uptake. This could influence the intensity and duration of their pharmacological effects and leads to errors in estimating pharmacokinetic parameters[1]. The purpose of this study was to investigate, using a double indicator dilution technique, the pulmonary first-pass uptake of theophylline in ventilated patients for extra pulmonary causes.

Materials and methods : After institutional approval and informed consent, ten patients (age 34-76 yrs), artificially ventilated for extrapulmonary diseases were studied. Following insertion of femoral arterial line and central venous catheter (CVC), a freshly prepared mixture of 10 mg of indocyanine green (ICG) and 60 mg of theophylline (Th) was administred as a single injection via the CVC. Immediately after, arterial blood samples were collected at 1-sec intervals into 45 heparinized tubes. In each sample, ICG concentration was measured spectrophotometrically at 805 nm, and Th concentration by fluorescence polarisation immunoassay technology (TDx®, Abbott). After extrapolation of the downslope of dye and Th dilution curves, mean transit time (Tm), cardiac output (CO), central blood volume (CBV) and Th pulmonary extraction (TPE) were calculated using a standard formula[2].

Results and discussion : Results are grouped (mean ± SEM) in table I.

C.O.(L/min)	Tm ICG (sec	CBV (L)	TPE (%)
4.73 ± 0.56	17.2 ± 1.6	1.27 ± 0.10	30 ± 1.5

Figure 1 describes the evolution of mean (±SEM) arterial concentrations of theophylline and ICG for all patients, after artificial standardisation of lag-time at 6 sec.



So, in patients with healthy ventilated lungs, the mean pulmonary first-pass uptake of Th is about 30% of the injected dose. Even these results does not permit to differentiate single pulmonary binding from pulmonary metabolism of Th, they have to be taken in account during pharmacokinetic calculations. More, further studies could show that, in case of pulmonary diseases, this Th lung uptake is different. This could explain the wide differences observed with Th pharmacokinetics in critically ill patients.

Conclusion : Many factors influence the Th pharmacokinetics in critically ill patients. Persistant difficulties in predicting appropriate injected dose emphasize the need to explore new factors. Pulmonary first-pass uptake could be one of these.

References: 1. Anesthesiology 71:62-68, 1989
2. Comp Progr Biomed 9:135-140, 1979

Sponsoring: CNEP INSERM

A.164

KINETICS OF INTRANASAL COCAINE FOR TOPICAL ANAESTHESIA IN NASAL SURGERY.

Eric Le Pelley*, Edouard Ferrand*, J.Michel Klossek**,Serge Bouquet***, Jacques Fusciardi*

(*) Department of anaesthesiology and intensive care, (**) Division of otolaryngology, (***) Laboratory of pharmacokinetic, University of Poitiers, 86000 Poitiers, France.

Background and goal of study: Because cocaine is a local anaesthetic and a vasoconstrictor, it remains widely used for otolaryngeal surgery. Kinetics of intranasal administration is known in healthy volunteers, but is fairly known in surgical patients. The aim of this study was to determine the pharmacokinetics of intranasal cocaine, used as the main anaesthetic agent for nasal surgery.

Materials and methods: After written informed consent 12 patients, ASA I or II, scheduled for medium meatotomy, or ethmoidectomy with topical anaesthesia only, were studied. Premedication was 100mg hydroxyzine orally 60', before surgery. After 2mg midazolam and 50µg fentanyl, 580µl aqueous 33% cocaine HCL(180mg) with moistened cotton tipped applicators were applied in each nasal cavity. Venous blood samples were drawn before cocaine application, 15,30,45,60,90,120,150,180 and 240 minutes after application. The concentration of cocaine was measured by HPLC. An anaesthesiologist looked for toxic effects (tackycardia,hypertension, cardiovascular collapse,mydriasis,agitation,irritability, mood lability, convulsion and vomiting).

Results and discussion: The mean dose(±SD) effectively given was 4±1.5mg.kg-1. No clinical evidence of systemic toxicity was found. Pharmacokinetics data are shown in the table. These results conflict with those found in healthy volunteers for two reasons : (i) our Tmax is shorter than Tmax observed with higher doses; (ii) there is not correlation between plasma concentration and physiological effects(1). However these results are closed to those previously described in surgical patients(2), except for Tmax, Cmax and half live. Higher Tmax in our study might be related to higher concentration of cocaine, which might decrease its own resorption because of vasoconstriction. In addition, these results, and subsequent clinical use in more than 1000 patients, suggest that a dose of 4mg.kg-1 may be safely used if the concentration is elevated(33%).

References: 1.Wilkinson et al.Clin.Pharmacol.Ther. 27:386-94,1990. 2.Bromley et al.Anaesthesia,43: 356-8,1988.

	applied dose mg/kg	effective dose mg/kg	area under curve µg/ml /min	Cl/F ml/min	Vd/F l	T1/2 min	Tmax min	Cmax ng/ml
mean	5.85	4	94	4521	568	86.8	47	859
SD	1.30	1.5	41	1869	273	19.3	17	503

A.165

DIRECT TOXICITY OF FLUORIDE IONS ON HUMAN KIDNEY CELLS

M.L. Cittanova, M.D., F. Wahbé, M.D., D. Prié, M.D., P.M. Ronco, M.D., P. Viars, M.D.
Département d'Anesthésie, Groupe Hospitalier Pitié-Salpêtrière and INSERM U64,Hôpital Tenon,Paris,France

Halogenated anaesthetics may induce a urinary concentration defect related to fluoride ion (FI) toxicity on the ascending limb of Henle's loop (ALHL). However, studies on the cellular mechanisms of FI cytotoxicity are hampered by the lack of appropriate in vitro models using ALHL cells of human origin. In the present work, we have analysed the deleterious effects of FI on a human tubular cell line immortalised by transfection with a plasmid containing a defective SV40 virus genome.

Methods : The cell line under study has kept the main characteristics of ALHL cells, including expression of the Na-K-2Cl cotransporter, involved in urinary concentration mechanism. Cells were cultured to subconfluency for 6 days at 37°C in hormonally defined medium, supplemented or not with increasing FI concentrations during the last 24 hours of culture. Cell injury was evaluated by measuring protein content , LDH release,and ^{3}H leucine incorporation. Effects of FI on sodium transport were analysed by assessing Na-K-2Cl cotransport (bumetanide-sensitive ouabaine resistant ^{86}Rb influx) and Na+-K+ATPase activity (ouabaine-sensitive Rb influx).

Results: Protein content, ^{3}H leucine-incorporation and Na-K-ATPase activity were significantly decreased and LDH release increased by FI concentrations >5 mM whereas Na-K-2Cl cotransporter was already inhibited at 1 mM.

FI concentration mM	0	1	5	10
LDH (UI)	44 ± 3	46 ± 8	148* ± 25	230* ± 24
Protein content mg.ml^{-1}	1.05 ± 0.15	0.95 ± 0.15	0.70* ± 0.20	0.45* ± 0.15
^{3}H Leu.inc cpm.g^{-1}.min^{-1}	60 ± 10	64* ± 14	30* ± 7	7 * ± 3
Na-K-ATPase nM.mg^{-1}.min^{-1}	27 ± 8	27 ± 13	12* ± 4	10 * ± 3
Na-K-2Cl nM.mg^{-1}.min^{-1}	15 ± 5	10* ± 4	1* ± 1	0* ± 1

* $p < 0.05$; m ± SD ; Newman-Keuls.

Discussion : The well differentiated human cell line used herein provides a useful tool for toxicity studies of fluorinated anaesthetics. Since FI are concentrated within the kidney (50-100 fold), FI concentrations tested may be clinically relevant. The fact that Na-K-2Cl activity was affected by lower concentrations than other parameters, suggests that this transporter is a major target of FI toxicity, which probably explains the urinary concentration defect and may be responsible for cellular abnormalities.

A.166

PLASMA INORGANIC FLUORIDE ION LEVELS FOLLOWING SEVOFLURANE ANAESTHESIA.

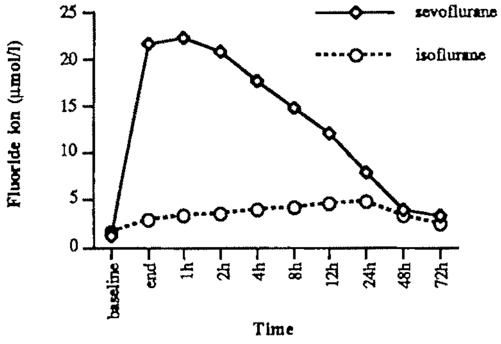
Newman PJ, Quinn AC, Hall GM, Grounds RM.

St George's Hospital, London, England.

The volatile agent sevoflurane is metabolised to inorganic fluoride ions which are potentially nephrotoxic in levels greater than 50μmol/l (1).

Methods: In a prospective, randomised study we compared the intra- and postoperative plasma fluoride ion levels and renal function in 50 ASA I-III patients following sevoflurane and isoflurane anaesthesia for major gynaecological and abdominal surgery. The anaesthetic technique was the same for both groups. Plasma fluoride ion levels were measured pre, intra- and postoperatively. Renal function was estimated by plasma urea and creatinine and plasma and urine osmolality pre and postoperatively at 24, 48 and 72h. The plasma fluoride ion concentrations were analysed using an ion selective electrode.

Results: There were no significant differences in patient demographic details, duration of surgery (range:50-350min) and type of operation between the groups. Mean MAC hr values were 0.8 for sevoflurane and 1.1 for isoflurane ($p<0.05$)



Plasma fluoride ion concentration against Time

The highest peak fluoride ion level was 40.4μmol/l in the sevoflurane group; there was no significant rise in the isoflurane group. In the sevoflurane group, fluoride levels peaked at 1h post operation and remained significantly higher than the isoflurane group until 48h later. No patient developed any significant decrease in renal function.

Discussion: Peak fluoride levels of >50μmol/l have been noted after prolonged sevoflurane anaesthesia (2). We used sevoflurane as part of a balanced anaesthetic technique and peak fluoride ion levels did not reach 50μmol/l even following 6h of sevoflurane.

References:
1.Cousins MJ,Mazze RI. JAMA 1973;225:1611-6.
2.Kobayashi Y et al. Anesth Analg 1992;74:753-7.

A.167

PROPOFOL BINDING IN HUMAN BLOOD

P. Altmayer, U. Büch, H.P. Büch, R. Larsen

Klinik für Anaesthesiologie und Intensivmedizin, Universität des Saarlandes, D-66421 Homburg/Saar

Background: Many studies with propofol were performed to establish pharmacokinetic parameters, as rational for adjustment of dosage regiments of this intravenous anaesthetic. Only few informations are available about the binding of this phenolic hypnotic to proteins. In the present study the binding of propofol to human fresh plasma, hemoglobin and serum albumin was investigated.

Material and methods: Propofol concentration was measured using a new high-performance liquid chromatography method (1). Equilibrium dialysis was carried out at room temperature (20 °C) in cylindrical glas chambers (d = 5 cm, volume 20 ml) with 1/15 M phosphate buffer (pH 7.4). It could be shown in preliminary experiments that propofol did not bind to the membrane used and after 8 hrs equilibrium of propofol concentration in both chambers was reached.

Results and discussion: Propofol binding to plasma over the large concentration range from 0.04 to 150 μg/ml was independent on the substrate concentration and amounted 97.4 - 98.6%. Serum albumin and hemoglobin also showed a marked binding for propofol. A 4 % solution of albumin bound 88.7% and hemoglobin 86.2% of the anesthetic. In studies with constant protein concentration and variation of the propofol concentration a decrease of the percentage bound with increasing substrate concentration was seen for hemoglobin, indicating saturable binding sites. The opposite was found for the interaction between propofol and albumin: increase of the binding extent with increasing substrate concentration. It is assumed that the highly lipophilic phenolic anesthetic is unspecifically associated with hydrophobic regions at the albumin molecule. As a result of this association conformational changes of the macromolecule may be induced and by that mechanism further hydrophobic places would be exposed with consecutive increased binding capacity.

References:
1. Altmayer P, Büch U, Büch HP, Larsen R: Rapid and sensitive precolumn-extraction HPLC assay for propofol in biological fluids. J Chromatogr 612: 326-330, 1993

A.168

EFFECT OF PROPOFOL ON HEPATIC BLOOD FLOW IN HUMANS

M. Ziehmer, U. Grundmann, J. Kreienmeyer,
P. Altmayer, R. Larsen

Klinik für Anaesthesiologie und Intensivmedizin, Universität des Saarlandes, D-66421 Homburg/Saar, Germany

Background: It is known that inhalational anaesthetics dose dependent alter total hepatic blood flow (HBF) in animals and humans, e.g. halothane decreases the total hepatic blood flow and the O_2-delivery to the liver to an greater extend than isoflurane at comparable concentrations. Besides changes in the global hemodynamic parameters cardiac output (CO) and mean arterial blood pressure (MAP) also direct vascular effects on the liver circulation are discussed as possible mechanism. The aim of the present study was to examine the effect of the intravenous anaesthetic propofol on liver blood flow with the particular view on possible hemodynamic correlations.
Material and methods: After institutional approval and informed consent the study was performed in 10 male patients (ASA I) undergoing minor orthopaedic surgery. HBF was measured by the indocyanine green (ICG) clearance method, CO noninvasively by the thoracic electrical bioimpedance method and systemic arterial blood pressure by an automated noninvasive device based on the oscillometric principle. In the awake state the cardiocirculatory parameters were registered, ICG (0.3 mg/kg) was injected and blood samples were taken at 2,4,6,8,10,12,14 min from a contralateral vein. Anaesthesia was induced with 2.5 mg/kg propofol and 2 µg/kg fentanyl. The patients were intubated and normoventilated with O_2/air (FiO_2:0.4) under control of the endexpiratory CO_2, anaesthesia was maintained by constant rate infusion of 8 mg/kg/h propofol. 30 min after the beginning of the propofol infusion a second bolus of ICG was given and blood samples were withdrawn. ICG concentration in serum was determined photometrically at 800 nm and the ICG clearance was calculated by the area under the curve.
Results and discussion: After induction with propofol CO decreased from 8.3 to 5.5 l/min, mean arterial blood pressure (MAP) from 99 to 79 mmHG and heart rate from 63 to 55 bpm ($p<0.01$). The total hepatic blood flow as determined by the ICG clearance decreased from 1167 to 824 ml/min under propofol, whereby the volume of distribution of ICG remained unchanged. A correlation between arterial blood pressure and HBF during propofol anaesthesia could not be seen.
Conclusion: The decrease of the liver blood flow seen under propofol anaesthesia is most likely due to altered systemic hemodynamic parameters and not a direct vascular effect of this phenolic hypnotic on the liver circulation.

A.169

TITLE: PROPOFOL-ALFENTANIL AND ISOFLURANE-ALFENTANIL ANESTHESIA FOR MAJOR THORACIC SURGERY

Authors: G.I.Bardoczky MD, M.Levarlet MD,
P.deFrancquen MD, A.d'Hollander MD, PhD.

Affiliation: Erasme University Hospital, Brussels, Belgium

INTRODUCTION: The study was designed to compare propofol-alfentanil (PA) and isoflurane-alfentanil (IA) anesthesia during lung surgery and assess the influence of the type of anesthesia on the first 16 postoperative hours.
MATERIALS AND METHODS: After IRB approval and informed consent 30 patients were randomly assigned in two groups.Prior to induction of anesthesia, an epidural catheter was inserted at the lumbar level. No analgesic was given via the epidural route during the surgery. Patients in group PA (n=15) received 1 mg/kg induction dose of propofol followed by a continuous infusion of the same drug at 6-10 mg/kg/hr until skin closure. In group IA (n=15) patients were given 0.2 mg/kg etomidate, and anesthesia was maintained with 0.5-1.5% isoflurane. FiO_2 was 0.4 - 0.6: N_2O was not administered. Pancuronium was used to intubate with the DLT. In both groups, alfentanil (A) infusion was started and maintained at 60 µg/kg/hr. 7 µg/kg A was given when MAP or HR increased by 15% of baseline. At the end of surgery, residual neuromuscular blockade was antagonized, 40% O_2 was given via face mask during the transport and stay in the ICU. Throughout the study period, MAP, HR, SpO_2, RR, FiO_2, $EtCO_2$ were recorded continuously with the Cardiocap and Capnomac monitors (Datex, Finland) interfaced with a computer. Arterial and venous blood gas samples were analysed to assess gas exchange. Continuous epidural fentanyl infusion was started postoperatively, at the request of the patient. The quality of recovery was assessed hourly with the modified Steward's recovery scores(1). Student t-test and Wilcoxon ranked sum test were used to analyse the data, $P< 0.05$ was significant.
RESULTS AND DISCUSSION: There were no significant differences between the groups with respect to demographic characteristics, intraoperative and postoperative MAP, HR, PaO_2, $PaCO_2$ $EtCO_2$ and SpO_2, but the postoperative lactate level was higher in the IA than in the PA group. The total dose and number of A boluses were similar in the two group. During emergence, 5 pt in the IA, and 2pt in the PA group had hypertension, 2 pt in the IA group had increased HR. None of the patients in the PA group experienced nausea, or vomited; in the IA group nausea was reported on 7 occasion, and 3 patients vomited. The PA group achieved and maintained higher recovery scores earlier than the IA group.
CONCLUSIONS: PA anesthesia showed similar hemodynamic and respiratory characteristics in the perioperative period than IA, and it seems to be a valuable choice for thoracic surgery. Earlier and more pleasant recovery may increase patient's motivation for deep breathing exercises and physiotherapy.

Ref.: 1.Can Anesth Soc J 1975: 22: 111-3.

A.170

PROPOFOL AND VOLATILE ANAESTHETICS

U. Grundmann, M. Ziehmer, J. Kreienmeyer, R. Larsen, P. Altmayer

Klinik für Anaesthesiologie und Intensivmedizin, Universität des Saarlandes, D-66421 Homburg/Saar, Germany

Background: Propofol gains increasing popularity for induction as well as for maintainance of general anaesthesia. Under certain clinical conditions anaesthesia by constant rate infusion with propofol is supplemented with volatile anaesthetics. In the present study the effects of the combination of propofol and halothane or isoflurane on haemodynamic parameters and serum propofol concentrations were investigated.

Materials and methods: After approval of the ethics committee and informed consent 20 healthy male patients undergoing elective orthopaedic surgery in general anaesthesia were studied. After induction of anaesthesia with propofol 2,5 mg/kg the patients were intubated and ventilated with oxygen/air (FiO_2:0,4). Anaesthesia was maintained by continuous infusion of propofol 8 mg/kg/h. After 45 minutes administration of propofol either 1 MAC halothane or isoflurane was commenced in 10 patients each. Every 5 minutes heart rate, blood pressure (automated oscillometric device) and cardiac output (thoracic electrical bioimpedance method) were measured non invasively and blood samples were taken for determination of propofol concentrations. Serum propofol concentrations were determined by means of HPLC.

Results and discussion: After induction of anaesthesia with propofol cardiac index decreased by 37 %, arterial blood pressure by 18 % and heart rate by 9 %. Constant serum propofol concentrations were achieved after 25 minutes with a mean concentration of 5.3 µg/ml. The addition of halothane resulted in a further significant decrease of the cardiac index by 10 %, whereas mean blood pressure remained unchanged. The propofol serum concentration increased to 6.5 µg/ml. A significant correlation was found between percentage changes of arterial blood pressure and changes of serum propofol concentration. If isoflurane was administered, blood pressure decreased by 10 %. cardiac index was not changed whilst the heart rate increased by 20 %. As in the halothane group serum propofol concentration increased to 6.4 µg/ml, but this changes did not correlate with any haemodynamic parameter.

Conclusion: Supplementing a propofol anaesthesia with halothane or isoflurane results in a rise of the serum concentration of this hypnotic, which may enhance its anaesthetic effect.

A.171

EARLY CORTICAL AUDITORY EVOKED POTENTIALS DURING SEDATION WITH PROPOFOL

BR Baxendale, DT Knights, and AR Aitkenhead.
University Department of Anaesthesia, Queen's Medical Centre, Nottingham NG2 7UH. UK

Background: Early cortical auditory evoked potentials (AEP) have been reported during maintenance of anaesthesia with propofol [1]. We aimed to investigate to what extent similar changes occurred during sedation with propofol.

Methods: Six healthy male volunteers aged 25-34 yrs (mean 30.1) were studied. After obtaining intravenous access, a baseline AEP was recorded, and the best reaction time to a distinct auditory stimulus noted. A propofol infusion was commenced using a step-down infusion scheme until the reaction time had consistently doubled from baseline. The AEP recordings were repeated. The propofol infusion was then increased until the reaction time had trebled, and the AEP recorded. All subjects had continuous monitoring of the ECG, pulse arterial oxygen saturation, and non-invasive blood pressure. Oxygen 4 l/min was delivered via nasal cannulae throughout. The AEP recordings used vertex (positive) and mastoid (negative) electrodes. Binaural auditory clicks of 0.4ms duration were presented at 6.38Hz and 75dB above the average threshold for the population. Noise levels were reduced on 1024 sweep averages using a high-pass filter of 30Hz.

Results: Significant changes in amplitude and latency of the early cortical AEP waveforms were demonstrated when the reaction time for subjects had doubled, and these persisted when reaction time had trebled (Table 1).

Table 1: Changes in the AEP variables during sedation with propofol. Values shown as mean (SD).
* = $p < 0.05$ (Student's t-test). RT = reaction time.

Latency (ms)	Baseline	RTx2	RTx3
Pa	30.3(3.6)	34.3(3.6)	30.2(3.0)
Nb	45.8(4.7)	52.8(4.2)*	55.0(5.6)*
Pb	61.7(6.8)	72.8(9.8)*	76.7(7.8)*
Nc	80.8(10.6)	95.2(14.1)	101.0(9.5)*
Amplitudes (µV)			
Pa	1.41(0.43)	1.02(0.22)*	1.13(0.42)
Nb	1.21(0.45)	0.80(0.19)	0.70(0.19)
Pb	1.12(0.45)	0.75(0.16)	0.52(0.10)*
Nc	0.99(0.29)	0.63(0.21)*	0.42(0.13)*

Conclusions: We have demonstrated that changes in latency and amplitude of early cortical AEP waves occur during sedation with propofol, although they are not of the same magnitude as during general anaesthesia.

References: 1. Thornton C. et al. *British Journal of Anaesthesia.* 1989;**63**:411-417.

A.172

THE SUBJECTIVE EFFECTS OF LOW-DOSE PROPOFOL.

C Whitehead, L D Sanders, G Oldroyd, T Haynes, R W Marshall*, M Rosen, J O Robinson[Ψ].

Departments of Anaesthetics and Pharmacology*,
University of Wales College of Medicine and the School of Psychology[Ψ], University of Wales College of Cardiff,
Cardiff, UK.

Background: Anecdotal reports suggest that patients anaesthetised with propofol not only recover rapidly, but often experience an increased sense of well-being on waking There have been descriptions of unusual emergences when propofol was one of the anaesthetic agents involved. These have varied from amusingly amorous or disinhibited experiences to disturbing dreams and reports of hallucination of sexual assault(1). This double-blind, placebo controlled study was designed to assess the effect of sub-anaesthetic concentrations of propofol on performance and mood. Approval was obtained from the local ethics committee.

Methods: Twenty-eight healthy male volunteers, after giving informed consent, were randomly allocated to one of three propofol infusions or placebo. The infusion rates were determined from a computer model to produce steady state plasma concentrations of 0.3, 0.6, and 0.9mcg ml^{-1}. At steady state the subjects performed six standard psychometric tests consisting of 2 objective measures (choice reaction time {CRT} and saccadic eye movement {SEM}) and four subjective measures (Spielberger Anxiety Inventory, Bipolar Profile of Mood States, VAS of Sedation, and the Addiction Research Center Inventory). Experienced observers rated the degree of sedation from videos of each subject with and without the sedative infusion.

Results: Statistically significant concentration related differences were observed with both of the objective tests (SEM, $p<0.001$, CRT, $p<0.05$). However no significant differences from placebo were detected by the subjective measures. The observers rating failed to detect a consistent drug related sedative effect.

Conclusion:

The results clearly demonstrate that the subanaesthetic doses of propofol achieved had significant effects on psychomotor performance but had no detectable effect on mood. The results of this study do not support the anecdotal reports of euphoria or other mood changes associated with low concentrations of propofol.

Reference:

1. Schaefer H, Marsch S. An unusual emergence after total intravenous anaesthesia. *Anaesthesia* 1989; **44**: 928-929.

A.173

SEDATION WITH PROPOFOL DOES NOT INTERFERE WITH GASTRIC EMPTYING

A Hvarfner, B Hammas, S-E Thörn, M Wattwil, Department of Anesthesia and Intensive Care, Örebro Medical Centre Hospital, S-701 85 ÖREBRO, Sweden.

Background & goal of the study: Delay or suspension of gastric emptying may result in nausea and vomiting. The incidence of postoperative nausea and vomiting is low after anestesia with propofol. The aim of this study was to examine the effect of propofol sedation upon gastric emptying and orocaecal transit time (OCT).

Subjects & methods: Ten healthy volunteers were examined at two different occasions. Gastric emptying was examined by absorption of paracetamol (acetaminophen), and OCT was determined through determinations of end-tidal hydrogen after ingestion of raffinose (1). Paracetamol is not absorbed from the stomach, but is rapidly absorbed from the upper small intestine, therefore the rate of gastric emptying determines the rate of absorption of paracetamol. The trisaccaride raffinose is not fermented until it reaches the caecum, where it is fermented by bacteria, resulting in production of hydrogen, whereby an increase in end-tidal hydrogen concentrations indicates arrival to the caecum. After randomization the volunteers were given a continous infusion of propofol at one occasion, and an infusion of saline at another occasion. Propofol was titrated to a sedation rate of 2-3/5, corresponding to a state of resting with closed eyes, but yet awakeable by light verbal address. This state was achieved by 2.4±0.7 mg/kg/h of propofol. After the induction of sedation the subjects ingested 2 g paracetamol and 10 g raffinose, followed by venous sampling at regular intervals for two hours for determinations of paracetamol concentrations. End-tidal determinations of hydrogen were performed every 15 minutes until a significant increase was seen.

Results: During propofol the maximum concentration of paracetamol (C_{max}) was 115±8.5 µmol/l (x±SEM), time to peak concentration (t_{max}) 50±12 min, and area under the curve during the first 60 minutes (AUC_{60}), 4793±486 µmol *x* min/l, versus C_{max} 99±6.6, t_{max} 69±42, and AUC_{60} 3897±414 during saline infusion. These differences between the occasions were not statistically significant. OCT was somewhat prolonged during propofol sedation, 217±21 min, versus 180±10 min during placebo infusion ($p=0.04$).

Conclusion: Sedative infusion of propofol does not interfere with gastric emptying and gives a minor increase in the orocaecal transit time. The absence of significant effects on gastrointestinal motility by propofol indicates that the antiemetic effect is rather a central effect, although it can not be excluded from this study that propofol might antagonize negative perioperative effects on gastrointestinal motility.

Reference: 1. T Thorén et al. Acta Anaesthesiol Scand 1989;33:174-180.

A.174

INFUSION OF PROPOFOL vs SUFENTANIL - MIDAZOLAM FOR SEDATION FOLLOWING AORTIC SURGERY

D. Amsellem, A. Ducard, G. Godet, J.P. Cornet, M. Ismail, P. Coriat, P. Viars
Département d'Anesthésie-Réanimation, G.H. Pitié-Salpêtrière, 75003 Paris, France

The practice of sedating and ventilating patients following abdominal aortic surgery (AAS) until they are normothermic is well admitted. Sufentanil (S) infusion has been shown to limit the incidence of post operative myocardial ischemia after coronary surgery (1). Propofol (P) has a more suited pharmacologic profile, and has been recommended for short medium and long-term sedation in ICU patients.

This study was designed to compare hemodynamic effects of S vs P when administered by continuous infusion for sedation following AAS.

Methods : A standardised anaesthetic technique was used in the 22 (11 vs 11) pts studied. At the end of the surgical procedure P vs S were compared in an open randomised study. The infusion rates were P : 2 mg/kg/h and S : 0,25 mcg/kg/h. In the S group, additional bolus doses of midazolam (2 mg) were given when needed to maintain a predetermined level of sedation (grade 2-5 on the Ramsay scale). Since our intention was to extubate the patients at central body temperature = 36°C, P and S infusion were stopped at different times, when central temperatures were respectively 36°C and 35°C. We prospectively defined the indications for postoperative cardiovascular therapy aimed at controlling blood pressure (BP) and HR during the study period.

Results : The two groups were similar as regards. 1) central body temperatures at the end of surgery (34,1 vs 34,1°C) and at extubation (36,7 vs 36,8°C), 3) The time from the end of surgery to patient extubation (225 ± 21 vs 224 ± 26 min). The time from stopping sedation to patient extubation were (p = 75 ± 48 vs 130 ± 50 min).

The desired level of sedation was obtained in all patients group S (in 7/10 cases with additional midazolam, and in 9/11 pts group P (sedation to deep in 2 cases). The need for postoperative cardiovascular treatment (P = 4/11, S = 9/11), and the maximal SBP (147 ± 5 vs 169 ± 6 mmHg) and HR (77 ± 4 vs 99 ± 5) noted until extubation are significantly higher in the S group ($p < 0,05$ vs P group).

Discussion : Our study demonstrated that continuous infusion of P or S (supplemented by midazolam) provides adequate level of sedation in patients following aortic surgery. However, P sedation was associated with a significantly lower incidence of hemodynamic abnormalities which are known to provoke postoperative myocardial ischemia.

(1) Mangano DT et al. Anesthesiology 76 : 342, 1992

A.175

PROPOFOL EFFECTS UPON APOMORPHINE INDUCED VOMITING

S-E Thörn, A Hvarfner, B Hammas, M Wattwil
Department of Anesthesia and Intensive Care, Örebro Medical Centre Hospital, S-701 85 ÖREBRO, Sweden

Background & goal of the study: Apomorphine, a dopamine agonist with potent emetic properties, has been used to empty the stomach prior to caesarean section (1). It has been proposed that propofol has an antiemetic effect even in non sedative doses (2).

The aim of this study was to investigate if propofol influences vomiting induced by apomorphine. Propofol was given both as a single non sedative dose and as a sedative infusion. Midazolam was given on an another occasion to evaluate the effect of sedation.

Subjects &methods: Ten healthy volunteers received apomorphine infusion (1 mg/min) until vomiting was induced on four different occassions in a randomized study: 1) during propofol infusion 2.4±0.7 mg/kg/h (mean±SD) at a sedation score 2-3/5, i e resting with closed eyes, although awakeble by light verbal address. 2) after a single dose propofol 0.4 mg/kg 3) during midazolam infusion 0.13±0.04 mg/kg/h at a sedation score 2-3/5 and 4) during infusion of saline (control).

Results: In order to provoke vomiting higher doses of apomorphine were needed during sedation with propofol (4.3±1.17 mg, mean ±SD) and midazolam (4.7±2.3 mg) ($p<0.001$), compared to the control situation with saline (2.5±0.54 mg). There were no significant differences between the sedative doses of propofol and midazolam. After the non sedation dose of propofol there was no significant increase (3.1±1.07 mg) in apomorphine dose needed to induce vomiting compared to the control situation.

Conclusion: Propofol given in a non sedative dose has no effect on apomorphine induced vomiting. However the total amount of apomorphine given to induce vomiting was significantly higher during propofol sedation. This was probably an effect of sedation as a similar result was achieved during midazolam sedation.

References: 1. Holdsworth JD, et al. Br J Anaesth 1974; 46:526-529, 2. Borgeat A, et al. Anesth Analg 1992; 74: 539-541.

A.176

PHARMACOKINETICS OF CLONIDINE AFTER RECTAL ADMINISTRATION IN CHILDREN

PA Lönnqvist MD DEAA *, HTG Bergendahl MD * S Eksborg PhD #

Department of Pediatric Anesthesiology & Intensive care, St Görans Pediatric Hospital, The Karolinska Institute (*) and Department of Pharmacy, The Karolinska Hospital and Institute (#), Stockholm, Sweden.

Introduction: The use of alpha-2 agonists have been shown to produce a number of desirable effects (e.g. reduced anesthetic requirements, increased intraop hemodynamic stability, postop analgesia without clinically significant respiratory depression) when used as premedication or as adjuncts to general anesthesia in adult patients (1). A number of these beneficial effects would be of great potential benefit in pediatric anesthesia. Only scant information regarding the use of alpha-2 agonists in children is currently available (2,3). The aim of this study was to investigate the pharmacokinetics of clonidine after rectal administration in children.

Methods: Ten ASA 1 pediatric patients (age range: 14-48 months, weight range: 10-20 kg) received 2.5 microgram/kg of clonidine by the rectal route. Blood samples were taken during a 24 hour period after the administration. Plasma levels of clonidine were analysed by radioimmunoassay and was subsequently subjected to a computer aided best curve fit program ($Nonlin^R$). In order to determine the bioavailability of clonidine the results from the present study was compared with data from a previously reported study where the same dose of clonidine was given to a similar patient population by the intravenous route.

Results: The following pharmacokinetic data were found [median value (95 % confidence interval)]: Maximum plasma concentration (Cmax): 0.77 nanogram/ml (0.62-0.88), time to Cmax was 51 min (29-70), terminal elimination constant (K_{el}): $9.21 \, . \, 10^{-4}$ ($5.92\text{-}13.22 \, . \, 10^{-4}$), and bioavailability 95 % (73-119). The K_{el} corresponds to a terminal half-life of approximately 12.5 h. Plasma concentrations within the clinically effective range were obtained within 20 min of administration.

Conclusions: The results indicate that the rectal administration of 2.5 microgram/kg of clonidine approximately 20-30 minutes prior to induction of anesthesia, at least from a pharmacokinetic point of view, appears to be suitable in children.

References: 1. Maze M, Tranquilli W. Anesthesiology 1991; 74: 581-605. 2. Mikava K et al. Anesthesiology 1992; 77: A1169. 3. Lönnqvist PA, Bergendahl H. Paediatric Anaesthesia 1993; in press.

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SEVOFLURANE *VERSUS* HALOTHANE IN PAEDIATRIC ANAESTHESIA

Tomi Taivainen, Olli A Meretoja, Pekka Tiainen,
Leena Räihä, Per H Rosenberg

Departments of Anaesthesiology,
Children's Hospital and Surgical Hospital,
University of Helsinki, Helsinki, Finland

Background and goal of study: Sevoflurane is challenging halothane, the leading volatile agent in paediatric anaesthesia. Our aim was to compare these agents in anaesthesia induction and recovery with special reference to hepatic integrity assessed by serum glutathione-S-transferase (GST).

Patients and methods: Following ethics committee approval and parental written informed consent, 50 elective 5-12 year old children (ASA 1-2) were randomized to receive either sevoflurane or halothane anaesthesia with no premedication. Face mask induction included N_2O:O_2 (2:1). Inspired sevoflurane was increased from 2 to 7%, and halothane from 1 to 3.5% with 3-5 breaths. Following endotracheal intubation, volatile agent was maintained at 1-1.2 MAC end-tidal concentration. In addition, fentanyl was administered for nociceptive reactions prn, and a dose-response curve of vecuronium was established in 30 patients. Induction and recovery parameters were monitored. Statistics included two-tailed t-test or Fisher's exact test. Values are mean ± SD.

Results: Patients averaged 9.0 ± 2.4 years and 33.3 ± 11.4 kg. Anaesthesia data are in the table. An ED_{95} of vecuronium was less under sevoflurane than under halothane (33 ± 9 *vs.* 41 ± 10 µg/kg, P<0.05). GST concentrations showed no intergroup differences.

Table. Anaesthetics, induction and recovery data

	Sevoflurane	Halothane	P
MAC-hours	2.0 ± 0.8	2.3 ± 1.3	NS
Fentanyl (µg/kg)	2.3 ± 1.2	1.8 ± 1.4	NS
Times (min) until			
- loss of eyelash reflex	1.0 ± 0.3	1.7 ± 0.6	<0.01
- end of induction	2.4 ± 1.0	3.3 ± 0.9	<0.01
- emergence	15 ± 12	33 ± 17	<0.01
- oriented for name	25 ± 11	43 ± 20	<0.01
Trieger points (max 52)			
- 1 h after anaesthesia	28 ± 14	15 ± 13	<0.01
24 h interview (%)			
- induction pleasant	56	20	<0.01
- same anaesthetic again	76	44	<0.05

Conclusion: Sevoflurane provided faster induction and recovery compared to halothane. Children appreciated sevoflurane more than halothane. Better acceptance may be due to non-pungency and rapid psychomotoric orientation with sevoflurane.

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COMPARISON OF INDUCTION AND RECOVERY CHARACTERISTICS OF SEVOFLURANE AND HALOTHANE IN CHILDREN

V. Piat, M.C. Dubois, I. Murat
Dpt of Anaesthesia, Hopital Armand Trousseau,
75571 Paris Cedex 12, France.

INTRODUCTION

Sevoflurane, a new inhalational agent, compares favourably with halothane for mask induction of paediatric patients as its smell is pleasant and it is non pungent. The present study was undertaken to compare induction and emergence characteristics of sevoflurane and halothane in children.

METHODS

After institution approval and informed consent, 29 children (9mo-9yr) scheduled for genitourinary ambulatory surgery were randomly allocated to receive either sevoflurane (SEVO, n=15) or halothane (HALO, n=14) for mask induction and maintenance of anaesthesia. Children were premedicated with 0.4 mg.kg-1 rectal midazolam. Induction was carried out by face mask using a mixture of O2 and N2O (40:60) and HALO or SEVO. The inspired concentrations used were successively 1%, 2%, 3% and 3.5% for HALO and 2%, 4%, 6% and 7% for SEVO. Inspired concentration was increased every 5 breaths unless clinical signs of respiratory complication were observed. Intubation was performed after placement of an IV line, then expired concentration was maintained at 1 MAC corrected for age until skin closure. Analgesia was provided by an epidural anaesthesia using a mixture of plain 1% lidocaine and 0.25% bupivacaine. Times to loss of eyelash reflex, intubation, extubation, emergence, response to verbal command and time for obtaining an Aldrete score ≥ 8 after discontinuing volatile agents were recorded. Comparison between groups used the Student t test. Results are mean ± SD.

RESULTS

The two groups were identical regarding age (HALO 57 ± 30 mo vs. SEVO 55 ± 31 mo), weight (HALO 19.4 ± 7.1 kg vs. SEVO 19 0 ± 7.7 kg), and time interval between induction and end of surgery (HALO 70 ± 24 min vs. SEVO 80 ± 24 min). Induction and recovery characteristics are indicated on table (* p<0.05;** p< 0.01; *** p<0.001). No respiratory complications were observed in the SEVO group, while 1 child had a mild laryngospasm in the HALO group.

parameter	halothane	sevoflurane
eyelash reflex (min)	1.9 ± 0.7	1.6 ± 0.6
intubation (min)	6.1 ± 2.0	5.7 ± 1.0
extubation (min)	19.2 ± 6.6	14.9 ± 1.6 *
emergence (min)	34.1 ± 11.1	18.6 ± 5.5 ***
verbal command (min)	46.6 ± 13.1	28.8 ± 8.4 ***
Aldrete score >7 (min)	35.7 ± 9.8	26.4 ± 6.1 **

DISCUSSION

These data confirm that sevoflurane is an acceptable alternative to halothane for induction of anaesthesia in children. Although sevoflurane is a less soluble agent than halothane, time to intubation was not different between groups in clinical practice. However, recovery was considerably faster as demonstrated by the decrease in time to extubation and other recovery parameters, suggesting that SEVO is suitable for outpatient anaesthesia.

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COMPARISON OF POST-OPERATIVE NAUSEA AND VOMITING AFTER THIOPENTONE / ISOFLURANE OR PROPOFOL INFUSION FOR 'BAT-EAR' CORRECTION IN CHILDREN.

W M Woodward, I Barker, J E Peacock

Sheffield University Department of Surgical and Anaesthetic Sciences, Royal Hallamshire Hospital, Sheffield S10 2JF, UK

BACKGROUND & AIMS: Correction of prominent ears is one of the commonest plastic surgical operations performed in children in the UK, and is usually carried out under general anaesthesia. As with other ear surgery, post-operative recovery is characterised by a high incidence of nausea and vomiting[1]. The aims of this study are a) to compare the incidence of nausea and vomiting following the use of propofol infusion or thiopentone / isoflurane, and b) to assess fitness for same-day discharge following each of these techniques.

MATERIALS & METHODS: After ethical approval, 30 healthy un-premedicated children aged from 4 to 14, (mean 10), yrs were randomly allocated to one of two groups. The patients, parents and nurses were blinded to the technique used. **Group I** received propofol 2.5 to 5mg/kg (with lignocaine 1mg/ml of propofol) for anaesthesia induction, followed by maintenance with propofol infusion in a step-down regime of 10, 8, and 6mg/kg/hr at 10 minute intervals. **Group II** received thiopentone 5 to 7 mg/kg for induction, and isoflurane 1 to 2% for maintenance. **Both groups** were supplemented with nitrous oxide 70% in oxygen and infiltration of the ears with a mixture of bupivacaine 0.25%, hyaluronidase, and adrenaline 1:200,000. Both groups were given atracurium 0.5mg/kg for tracheal intubation, and were mechanically ventilated to a $P_{E'}CO_2$ of 4.0 to 4.5 kPa. Neostigmine 0.05mg/kg, (with glycopyrrolate 0.01mg/kg), was used to reverse residual neuromuscular block at the end of surgery.
Duration of anaesthesia, and times to conscious response, ingestion, and mobilisation were recorded. Complaints of nausea and episodes of vomiting were recorded and a four-point pain score was indicated at 24 hours by patients and (independently) by the ward nurses. Analgesic requirements were recorded together with an assessment of fitness for discharge from hospital. Chi-square, Mann-Whitney-U, and t-tests were applied to the results as appropriate.

RESULTS & DISCUSSION: 3 of 15 children in Group I vomited in the first 24 hours, compared with 10 children in Group II, (p < 0.01). For those children vomiting, the number of episodes was also significantly greater in Group II, (p = 0.02). 1 child in Group I complained of nausea compared with 8 in Group II, (p < 0.01). Mean time from reversal to conscious response was 6.3 minutes in Group I and 11.7 minutes in Group II, (p < 0.05), but there were no other significant differences in recovery indices between the groups. 8 patients in Group I and 4 patients in Group II were considered fit for discharge on the day of surgery, (p = 0.09, ns). The remainder were all fit for discharge by the next day. Reasons for not being fit for discharge on the day of surgery were pain control only, (Group I), and pain control and vomiting (Group II).

CONCLUSIONS: 1)Propofol infusion for maintenance of anaesthesia for 'bat-ear' surgery in children is associated with significantly fewer emetic sequelae than when thiopentone and isoflurane are used. 2) Immediate recovery from anaesthesia is significantly shorter following propofol infusion, but the choice of technique does not influence subsequent recovery times. 3) Children may be fit for discharge on the day of surgery if pain is adequately controlled.

REFERENCE: [1] *British Journal of Plastic Surgery* 1973; **26**: 336.

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Original

ISOFLURANE AND THE NEUROMUSCULAR EFFECT OF MIVACURIUM IN PEDIATRIC PATIENTS.

C. Van Lersberghe,MD, F. Camu,MD, F. Christiaens,MD, P. Peeters,MD
Dept. Anesthesiology, Flemish Free University of Brussels, Belgium.

Background and goal of study : Mivacurium induces a short neuromuscular block (NMB) in children. But the effects of isoflurane, infusion administration and age on mivacurium NMB are unknown. This was studied in children of two different age groups during isoflurane and intravenous anesthesia.

Material and methods : Following approval by the University Ethics Committee and written parental consent, 20 children (age 2-12 yr) and 20 adolescents (age 13-17 yr) were studied. In each age group, the patients received either isoflurane (1-2%) in N_2O/O_2 anesthesia (ISO) or propofol-alfentanil and N_2O/O_2 anesthesia (TIVA). The thumb adductor m. compound EMG for train of four stimuli of the ulnar nerve was monitored. Following an intubation dose of 0.2 $\mu g.kg^{-1}$ for children and 0.15 $\mu g.kg^{-1}$ for adolescents, a mivacurium infusion was started at twitch recovery of 10% to maintain NMB between 80-90%. Recovery of NMB occurred spontaneously.

Results and discussion : Onset time and time to maximal NMB occurred later in the TIVA groups while maximal block was greater in the ISO groups. Spontaneous recovery after bolus dose was slower in adolescents despite a lesser NMB. Constant NMB required 20% higher infusion rates in the TIVA groups. Recovery after infusion was prolonged by 18% in children and 29% in adolescents receiving isoflurane. NMB recovered faster in children than in adolescents with both anesthesia techniques.

Conclusion : ISO potentiates the NMB by 20 to 30% in both children and adolescents compared to propofol anesthesia.

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REVIEW OF 253 EPIDURAL CATHETERS INSERTED AT THE LUMBAR OR THORACIC LEVEL IN CHILDREN LESS THAN 2 YEARS OLD.

D. Delbrouck, F. Veyckemans, F.J. Singelyn, L.J. Van Obbergh, J.M. Gouverneur.

Dept. Anesthesiology, UCL Medical School, Clin. Univ. St Luc, 1200 Brussels, Belgium.

Background : In young children, many authors nowadays recommend inserting epidural catheters (EC) up to the thoracic level using the caudal approach (1, 2). We routinely insert EC directly at the thoracic (T) or lumbar (L) level, as needed by surgery. In order to assess the safety of our practice, we retrospectively reviewed the records of all the children less than 2 years old who had an EC inserted at the L or T level from 1985 to 1992.

Material and methods : All the EC were inserted under general anaesthesia prior to surgery; either a 19G or a 18G Portex Minipack set was used. The epidural space was located by a median approach using the loss of resistance to saline technique. The initial dose of bupivacaine 0.25 % (0.5 or 0.75 ml/kg) contained epinephrine 1/200.000; a continuous infusion of bupivacaine 0.125 % (0.1 to 0.3 ml/kg/h), alone or with fentanyl 1 mcg/ml, provided postoperative analgesia. The anaesthetic records and the postoperative notes were reviewed : demographic and technical data concerning EC insertion and per- or postoperative complications were collected.

Results and discussion : A total of 253 EC were inserted during the study period : the distribution of the patients according to age and intervertebral space of EC insertion is given in the table. The EC was inserted at 1st attempt in 91.9 % and at a 2nd attempt in 4 5 % of cases, respectively. Another intervertebral space had to be used in 1.2 % of cases. No dural tap occurred. Blood was aspirated through the EC in 1.6 % of cases. Four children presented with hypertension and tachycardia during the first injection through a EC which had been easily inserted at 1st attempt with no evidence of vessel damage : these EC were removed. The epidural block was successful during surgery in 97.6 % of cases. The postoperative catheter-related complications were : disconnection (4.5 %), kinking (2.8 %), leakage around the EC (2.4 %), EC out (2 %). One child presented with jitteriness in the recovery room : aspiration through the EC, which had been easily inserted, was positive for blood and it was removed. The main patient-related problem was urinary retention (3/140 patients in whom no urinary catheter had been inserted for surgery) which quickly responded to transient interruption of the epidural infusion.

Conclusion : The safe use of T or L EC in young children requires technical expertise, but also careful clinical observation to avoid complications. We recommend using an epinephrine-containing local anaesthetic solution for each bolus dose in order to detect inadvertent intravascular injection.

Table :

age	intervertebral space				
months	> T10	T10-L1	L1-L4	?	Tot.
< 1	1	10	23	3	37
1-6	3	20	78	6	107
6-12	6	15	39	1	61
13-24	9	9	28	2	48
Tot.	19	54	168	12	253

References : 1) Anesthesiology, 76 : 935-938 (1992)
2) Can J Anesth 37 : 359-362 (1990)

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AFTER TRANSSACRAL EPIDURAL APPROACH, WHERE DO THE CATHETER GO ?

Eric Le Pelley, Nicolas Dalibon, Eric Urvoas*,
Anne-Marie Dubousset, Claude Ecoffey

Department of Anaesthesiology and Intensive Care, (*)
Department of radiology, University of Paris XI,
Kremlin-Bicêtre, France.

Background and goal of study : Described by Busoni in 1987, transsacral route is wise used in paediatric anaesthesia (1). After caudal or lumbar routes, the catheter 20G could be advanced at least to the thoracic level easily in infant (2,3). Now smaller catheter are available for paediatric regional anaesthesia. The aim of this study was to determinate the feasibility of placement of a 21G catheter at a lombo-thoracic epidural level via a transsacral route.
Materials and methods : Twenty seven children, ASA I or II, aged 1 month-5 years, undergoing surgery were studied. The children were scheduled for upper abdominal surgery and renal surgery. The protocol was approved by our hospital ethical committee. Children less than 6 months of age were not premedicated. The other received diazepam orally 0.3 mg.kg^{-1}, 1 hour before surgery. General anaesthesia was induced with nitrous oxide and halothane, after which an intravenous line was placed. Tracheal intubation, and ventilation was controlled by intermittent positive pressure ventilation. A small epidural catheter 21G Portex^{R} was introduced through a 19 G Portex^{R} Tuohy needle, at the sacral intervertebral space, as previously described by Busoni, in order to obtain intra- and postoperative analgesia. We recorded number of ponction, incidents, distance between skin-epidural space, resistance to climb up the catheter, catheter lenght in epidural space. At the end of surgery, a predertermined volume of iopamidol-a water soluble non-irritant radio opaque contrast medium-was injected slowly into the epidural catheter through a millipore bacterial filter to fill the catheter. In recovery room, abdominal radiograph was then taken to determine the exact path of the catheter and location of the catheter tip. We classified in three categories : no interpret because puddle of radio opaque contrast, climb, roll up.
Results and discussion : The epidural space was find at the first ponction in all patients.The introduction of catheter was always easy. In one child blood was noted during the introduction of the cannula, but no blood was aspirated from the epidural catheter. The distance of space from the skin could not be accurately predicted because it depends largely on the amount of fat overlying the sacrum. Analgesia during the surgery was excellent with 0.75 ml.kg^{-1} of 0.25% bupivacaine with adrenaline; in recovery room, not any child needed analgesic treatment. In 27 catheters, only 9 climbed in level wanted; 5 were no interpreted and 13 were rull up. **Conclusion :** When a small catheter, such as 21G size was used via the transsacral route in order to obtain thoracic dermatoms levels of analgesia, the catheter tip was in the right place in only 40% of patients. Therefore, the catheter tip should be checked routinely if the catheter is used for continuous postoperative analgesia.
References : **1.** Busoni P. et al. : Anesthesiology, 67 : 993-995, 1987. **2.** Bösenberg A.T. et al. Anesthesiology, 69 : 265-269, 1988. **3.** Ecoffey et al. : Anesthesiology, 65 : 87-90, 1986.

A.183

AXILLARY PLEXUS BLOCK FOR POSTOPERATIVE ANALGESIA IN CHILDREN

S. Gautschi-Meyer and A.Ch. Gerber
Department of Anaesthesia, University Children's Hospital, Zurich, Switzerland

Background and goal of study: The importance of good postoperative analgesia in children is increasingly appreciated. Several regional blocks lend themselves for this purpose. We investigated prospectively if axillary plexus block is suited for postoperative analgesia after surgery on the upper extremities. A catheter technique without nerve stimulation was chosen for its speed and simplicity.
Material and methods: In 113 children (4m-16y) 118 blocks were performed under inhalational anaesthesia (Halothane/N_2O/O_2). A 22G Abbocath was introduced in the neurovascular sheath of the axilla. Patients received 0.25% bupivacaine with adrenaline 0.5 ml kg^{-1} following a test dose. After surgery lasting $\geq$60 minutes additional 0.25 ml kg^{-1}, after $\geq$120 minutes additional 0.5 ml kg^{-1} of bupivacaine was injected and the catheter withdrawn. Postoperatively patients with signs of pain or discomfort were given systemic analgesics freely. Successful blocks were defined by evidence of neural blockade during and after surgery and no analgesic requirement for >2 hours. In partially successful blocks discomfort or pain was demonstrated despite evidence of neural blockade. In failed blocks no effect was detectable.
Results and discussion: From 118 blocks 95 (80.5%) were successful, 12 (10.2%) partially successful and 11 (9.3%) failed. From patients with successful blocks 40.0 % never required analgesics, 33.7 0% required analgesics later than 8 hours and 26.3 % between 2 and 8 hours after surgery. Unintended venous or arterial puncture occurred 26 times but never resulted in intravascular injection or haematoma. No case of nerve damage, infection or compartment syndrom was observed.
Conclusion: Axillary plexus blockade with a catheter technique is a simple and efficient method for providing prolonged postoperative analgesia in children after surgery on the upper extremities.
Reference: Selander D: Catheter technique in axillary plexus block. Acta Anaesth. Scand 1977; 21:324-329

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TITLE: PATIENT-CONTROLLED ANALGESIA (PCA) IN CHILDREN. - A COMPARISON OF AGE-RELATED POSTOPERATIVE MORPHINE-REQUIREMENTS.

AUTHORS: Tom G. Hansen, Steen W. Henneberg & Peter Hole.

AFFILIATION: Department of Anaesthesiology and Intensive Care. Odense University Hospital, DK-5000 Odense, Denmark.

BACKGROUND & GOAL OF THE STUDY: Since the introduction of patient-controlled analgesia (PCA) in children at our department 3 years ago, we have found that apart from providing excellent analgesia in the treatment of postoperative pain, PCA provides us with different "objective" information about children and pain perception. Especially, PCA can be used as an aid in the quantification of pain (1). It is still a widespread belief, that younger children require less morphine for postoperative analgesia than do older children and adults (2). In order to investigate this allegation we reviewed the charts of 28 children on PCA and compared the median age-specific morphine requirements between 2 groups of children aged 4 - 8 years and 9 - 15 years, respectively.

MATERIALS & METHODS: 28 consecutive children treated with intravenous PCA with morphine postoperatively, following major abdominal or orthopaedic surgery were reviewed and divided in 2 groups according to age. Group 1 consisted of 12 children aged 4 - 8 years, and group 2 of children aged 9 - 15 years. The 2 groups were comparable with regards to: type of surgery, surgical complications, sex, duration of PCA treatment and side-effects as well as the efficacy of the PCA treatment. The same type of pump were used in all children (Pharmacia-Deltec; CADD-PCA). The settings of the pump were the same: a bolusdose of 25 micrograms/kg, a look-out interval of 8 minutes without any background infusion. They all received paracetamol orally or rectally as a supplement to the morphine.

RESULTS & DISCUSSION:

	median morphine consumption (10-90th percentile) (micrograms/kg/hours)		
	0 - 12 hours	13 - 36 hours	total
group 1	10,5 (4,7-31,8)	14,8 (9,1-24,5)	11,6 (6,1-18,1)
group 2	8,3 (2,7-20.7)	12,2 (6,1-22,0)	7,5 (4,8-13,9)
P value *)	0,423	0,146	0,029

*) Mann-Whitney's two rank sum test.

In the present study, children aged 4 - 8 years had a higher total morphine requirement as compared to children aged 9 - 15 years during the entire postoperative period. It is unclear whether this is due to a true difference in requirements or merely a difference in the anaesthetic technique used, i.e. a more frequent use of regional anaesthesia and/or more liberal dosages of opioids intraoperatively in the older children.

CONCLUSION: Children aged 4 - 8 years had a higher total morphine requirement for postoperative analgesia following major abdominal or orthopaedic surgery as compared to children aged 9 - 15 years.

REFERENCES:

1. Gillespie JA, Morton NS. Patient-controlled analgesia in children: a review. Pediatr Anaesth 1992; 2: 51-9.
2. Lloyd-Thomas AR. Pain management in paediatric patients. Br J Anaesth 1990; 64: 85-104.

A.185

POSTOPERATIVE ANALGESIA IN CHILDREN AFTER ODONTOLOGIC PROCEDURE: A COMPARISON OF DICLOFENAC VERSUS KETOROLAC IN THE OUTPATIENT CLINIC

PREGO G.MD,MOSCOVICI R.MD,SCHWARTZ M.MD,STEINFELD O.MD, and GIL I. MD.

Department of Anaesthesia,Haemek Medical Center, Afula, Israel.

This study was designed to determine the relative analgesic efficacy of simple intramuscular injections of Ketorolac(1mg/kg) and Diclofenac(1mg/kg) in children undergoing odontologic procedure, under General Anesthesia in the outpatient clinic.

In a double-blind, controlled trial involving 75 healty children, undergoing odontologic treatment (multiple teeth removal). (Table I)

Medication for anaesthesia included,Nitrous Oxide and incremental doses of Halothane, Fentanyl and Atropine.

All patients underwent tracheal intubation facilitated with atracurium 0.5 mg/kg.

Patients were randomly assigned to one of two groups. One received Ketorolac 1 mg/kg im,and the second group received Diclofenac 1 mg/kg im, immediately after the induction.

At the end of the procedure neuromuscular blockade was antagonized and the trachea was extubated.

In the recovery room(RR)pain was evaluated by the child using a Visual Analog Scale (VAS)and by a blinded observer using both a VAS and a Objective Pain Scale (OPS)at 0, 2 and 4 hours after arrival in RR.

Postdischarge pain was assessed by telephone interview two times in the next 24 hours.

The Diclofenac group had the lower postoperative pain scores at all time points and did not require analgesia in the early postoperative period (one child felt discomfort in the first 12 hours).

In the Ketorolac group 7/38 patients in the first 2 hrs.and 12/38 patients in the first four hours required analgesia ($p < 0.05$)and had higher pain scores(this group had higher pain scores overall)

In conclusion Diclofenac i.m.provided better post operative pain control than Ketorolac in children undergoing outpatient odontologic procedures.

Table -I- Patient details-

		Ketorolac	Diclofenac
Number;n=	75	38	37
ASA		I	I
Age;yr	6.05(2.40)	6.02(2.61)	6.08(2.21)
Sex;M:F	45:30	23:15	22:15
Weight;kg	19.51(5.77)	19.39(5.56)	19.29(6.05)
Oper.Time:min.	50.06(17.50)	49.73(17.55)	50.40(17.69)
Dose im.	-----	1mg/kg	1mg/kg
Postop.time	hs		
n=No.of Patients	0	n=38	n=37
	2	n=31	n=37
not requiring	4	n=26	n=36
	12	n=23	n=35
analgesia	24	n=17	n=35

Values are expressed as mean (S.D.)

Reference:

Dahl J.B. and Kehlet H; Non - Steroidal anti-inflamatory drugs: Rationale for use in severe postoperative pain:British Journal of Anaesthesia 1991;66:703-712.

A.186

DIFFICULT INTUBATION IN CHILDREN : USE OF FIBEROPTIC BRONCHOSCOPE

JP MONRIGAL, JC GRANRY, C JEUDY, B ROD,
A DELHUMEAU
Department of Anesthesiology CHU ANGERS
49033 ANGERS Cedex 01 FRANCE

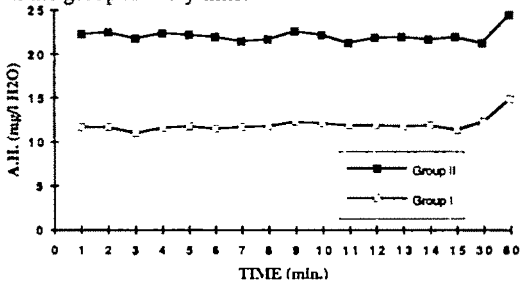
Aim of the study : We used a fiberoptic bronchoscope (FB) to evaluate the degree of difficulty in intubation and to perform it, especially in young children.
Material and methods : 120 patients were intubated with FB over a period of 7 years. age : 3 hours -> 15 years / weight : 1,5 -> 55 kg. We used a classic pediatric FB (external diameter 3.6 mm) : Intubation :
1. the internal diameter (ID) of the endotracheal tube (ET) is larger than 4 mm. => the ET is slipped on the FB which is introduced generally through the nare.
2. the ID is smaller than 4.5 mm. => the FB is passed through the vocal cords ; a guide wire is introduced through the operating channel of the FB, which is then removed. The ET is slipped along the guide wire (Stiles technic). Evaluation of the degree of difficulty in intubation : the tip deflection angle (TDA) is the value of the deflection of the tip of the FB to pass through the vocal cords. Up to 65° intubation will be easy ; from 65°to 75°a trained anesthesiologist will be required to intubate ; over 75° intubation by FB needed should be considered. The child is awake. We monitor the clinical signs and the SO2. Endoscopy and intubation are performed under local anesthesia (Lidocaïne 0,5 %, 1 $ml.kg^{-1}$) preceded by premedication (Midazolam by rectal route 0,35 $mg.kg^{-1}$) O2 is supplied by nasal route. The anesthesiologist who intubates the child is in front of him.
Results : Intubation was always possible and well tolerated locally (no spasmes or edema). Intubation was always performed rapidly (less than 2 min.) and on the first attempt ; with the Stiles technic many attempts (no more than 3) were necessary to complete intubation in some cases.The monitoring of the SO2 during the intubation showed brief, and no deep, decreases.
Discussion : It is a very efficient technic in case of difficult intubation, all the more so if it is performed on a patient who is awake. The measurement of the TDA seems a rapid and reliable technic to evaluate the degree of difficult intubation, especially in babies where the high position of the glottis is the most common cause of difficult intubation. Furthermore, clinical and radiological criteria of difficult intubation do not exist for young children. The anesthesiologist's position in front of the child simplifies the learning of intubation with a FB : the bending section is moved in only one direction.
Conclusion : Because the fall in SO2 is rapid, the local reactions are severe and frequent, the FB seems to be the best device to predict and perform difficult intubation in children.
Reference : Rucker R.W. et al : Fiberoptic bronchoscopic nasotracheal intubation in children.
Chest, 76:1, 1979.

A.187

INTEREST OF HEAT AND MOISTURE EXCHANGER DURING SHORT OPERATIONS IN YOUNG CHILDREN

MONRIGAL J.P., GRANRY J.C., JEUDY C.,
LE ROLLE T., DELHUMEAU A.
Department of Anesthesiology CHU ANGERS
49033 ANGERS Cedex 01 FRANCE

Aim of the study : To evaluate the possibilities of the heat and moisture exchanger (HME) to compensate, rapidly and efficiently, for the loss of heat and moisture in the airways of the young intubated and ventilated child.
Material and methods : The population of 40 children (age : 48±20 months, weight : 16±3,5 kg) for scheduled operations is divided into 2 groups : group I (n=20) without HME ; group II (n=20) with HME (Pall BB 25). The temperature and the relative humidity (RH) of the anaesthetic gases are monitored by a probe, located immediatly at the end of the endotracheal tube (E.T.) and before the HME in group II. The probe is connected to a computerized analyser (MPM 4000 Neotronics-Solomat) allowing measurement of the 2 parameters every 3 seconds. The body temperature, the temperature of the operating room, the ventilatory parameters (minute ventilation, peak inspiraty pressure, leakage, $ETCO_2$ by sidestream system) and the length of the E.T. protruding from the mouth are noted (children are ventilated with SV9000 D Siemens-Elema). From the values recorded, the lowest points of humidity and temperature, which correspond to insufflation phases, are extracted every minute during the first 15 minutes. The absolute humidity (AH) is calculated. The same analysis is performed at 30 and 60 minutes. The Student's test is used for statistical comparisons.
Results : There are no significant differences in the 2 groups concerning age, weight, body temperature or temperature of the operating room. No statistical differences are noted for the ventilatory parameters. However, the differences for the AH and the temperature of the anesthetic gases are statistically higher (p < 0,001) in the group II every time.



Discussion : The gain in humidity and airway temperature is immediate upon installation of the HME Pall BB 25 and remains stable for the duration of the operation.
Conclusion : It seems logical to use this HME even for short operations, in young children whose airways are very sensitive to heat and moisture conditions.
Reference : Passive and active inspired gas humidification in infants and children. Bissonnette B. Sessler D.I., Laflamme P. Anesthesiology 71, 3, 1989

A.188

INHALED NITRIC OXIDE IN CHILDREN-INITIAL EXPERIENCE

PA Lönnqvist *, P Winberg #, B Lundell #, GL Olsson *.
Depts of Paediatric Anaesthesia (*) and Paediatric Cardiology (#), St Görans Children's Hospital, Stockholm, Sweden.

Introduction: With the discovery by Frostell and Zapol that inhaled nitric oxide (NO) was capable of producing selective pulmonary vasodilatation both in animals and humans a growing number of reports have now been published regarding its use in adult intensive care medicine. The few reports regarding the use of inhaled NO in neonates and children with pulmonary hypertension have so far been very optimistic regarding the potential of this treatment in the paediatric patient category (1,2,3). The aim of this report is to present our initial experience with this new treatment modality in neonates and children.

Material: The administration of inhaled NO to neonates and children was approved by both the local ethical committee and the Swedish Medical Products Agency.

Fourteen paediatric patients (neonates 8, infants 5, child 1) with pulmonary hypertension of various ethiologies (CHD 3, MAS 3, CDH 2, Sepsis 2, BPD 2, various 2) were subjected to the exposition of inhaled NO (dose range: 20-80 ppm; duration of NO administration: 30 min-60 h). pO_2 and post-ductal oxygen saturation (SpO_2) were noted immediately prior to inhaled NO and compared to the best corresponding values achieved within sixty minutes of initiating the NO treatment.

Results: In ten patients inhaled NO increased pO_2 by > 1 kPa and/or increased post-ductal SpO_2 by > 10 % and in four of these patients pO_2 increased more than 3 kPa. In the remaining four cases the treatment had no effect on oxygenation. In six patients other intravenous vasodilators had been tried without any beneficial effect on gas exchange. Systemic arterial blood pressure was not affected by the administration of inhaled NO in any of the patients. Significant methaemoglobinemia (13.9 %) was found in one patient. The premature baby with a severe group B streptococcal sepsis suffered an intraventricular haemorrhage.

Discussion: This case series show that the initial enthusiasm (1,2,3) over this new drug must be somewhat more realistic. In conclusion, our results showed that inhaled NO in about one third of the patients produced a substantial effect which most likely significantly altered the course of the disease (possible to avoid ECMO in two cases). In another third of the patient inhaled NO only produced a moderate effect on oxygenation and in the last third the patients did not respond to the treatment. In no case where the patient already had radiographic signs of severe generalised pulmonary injury was inhaled NO capable of improving the patients condition. This indicates that inhaled NO should not be used as a last resort but instead in an earlier phase of the disease. In order to have the best opportunity to be successful with the use of inhaled NO we would like to propose to initiate this treatment at the point where one usually starts to contemplate the use of an intravenous vasodilator.

References: 1. Roberts JD et al. Lancet 1992; 340: 818-819. 2. Kinsella JP et al. Lancet 1992; 340: 819-820. 3. Kinsella JP et al. J Pediatr 1993; 123: 103-08.

A.189

INDUCTION OF ANAESTHESIA WITH SEVOFLURANE IN CHILDREN :HAEMODYNAMIC EFFECTS

M.C. Dubois, V. Plat, I Murat
Dpt of Anaesthesia, Hopital Armand Trousseau,
75571 Paris Cedex 12, France.

INTRODUCTION

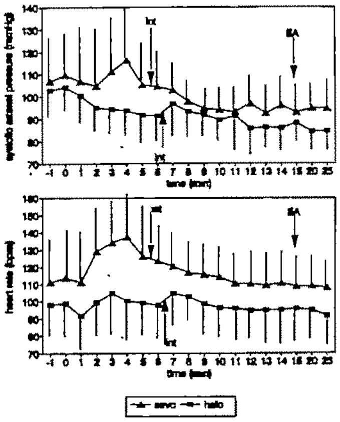
Sevoflurane, a new inhalational agent, is under clinical investigation in children. The present study was undertaken to compare the haemodynamic effects of sevoflurane and halothane during induction of anaesthesia in children.

METHODS

After institution approval and informed consent, 29 children (9mo-9yr) scheduled for genitourinary ambulatory surgery were randomly allocated to receive either sevoflurane (SEVO, n=15) or halothane (HALO, n=14) for induction and maintenance of GA. Children were premedicated with 0.4 mg.kg-1 rectal midazolam. Induction was carried out by face mask using a mixture of O2 and N2O (40:60) and HALO or SEVO. The inspired concentrations used were successively 1%, 2%, 3% and 3.5% for HALO and 2%, 4%, 6% and 7% for SEVO. Inspired concentration was increased every 5 breaths unless clinical signs of respiratory complication were observed. Intubation was performed after placement of an IV line, then end tidal concentration was maintained at 1 MAC corrected for age using mechanical ventilation. Analgesia was provided by an epidural anaesthesia (EA) using a mixture of plain 1% lidocaine and 0.25% bupivacaine. Systolic (SAP) and diastolic (DAP) arterial pressure and heart rate (HR) were measured every minute during induction for 15 min, then every 5 min. Results are mean ± SD.

RESULTS

The two groups were identical regarding age (HALO 57 ± 30 mo vs. SEVO 55 ± 31 mo), weight (HALO 19.4 ± 7.1 kg vs. SEVO 19.0 ± 7.7 kg), and time-interval between induction and skin incision (HALO 29.9 ± 5.4 min vs. SEVO 30.0 ± 7.5 min). Changes in SAP and HR during induction are shown on figures.



DISCUSSION

Induction with sevoflurane was characterized by an increase in SAP and HR that was maximal 4 min after introducing the agent in the breathing circuit. No haemodynamic changes were observed at the time of intubation in the SEVO group while children in the HALO group exhibited a small increase in SAP and HR.

A.190

ASTHMA IN PREGNANCY

E.Gollo,S.Treves,I.Castelletti,M.Fiaccavento
S.Anestesia e Rianimazione Ospedale S.Anna
Torino

Background & goal : asthma is a chronic inflammatory desease of airways that may induce a serious clinic sinptomatology. In pregnancy 0,4-1,3% of women are affected by this pathology. The international literature doesn't agree about pregnancy effects on asthma and asthma effects on pregnancy, while is well known that fetal outcome is negatively influenced by the desease, with increase in perinatal mortality and small weight newborns. Goal of this paper is the evaluation of the mutual interference between asthma and pregnancy and the investigation of maternal and foetal outcome.
Materials and methods : 50 pregnant asthmatic women and a control group of 50 randomised physiological pregnant women hospedalized - from January 1990 to 30 June 1993 - in the University Institute and S.Anna Obstetric Gynecologic Hospital of Turin, have been studied. All subjects gave informed consent to the study. The evolution of asthma during pregnancy is settled by pharmacological approach and by women's direct interview. Maternal outcome is studied looking at:

- basal conditions (asthma gravity)
- asthma evolution
- pregnancy evolution
- general versus regional anaesthesia

Neonatal outcome is evaluated looking at APGAR score at 1 and 5 minutes, weight at birth, eventual malformations, outcome and follow up.
Results:Asthma incidence in pregnancy women is shown [illegible]
The patients, at the beginning of pregnancy, have been divided into 3 groups: 32 cases of middle gravity, 15 cases of moderate gravity and 3 cases of severe gravity .
The evolution of disease is evaluated by pharmacological approach and by subjective synptomatology.
Neonatal associated pathology is discussed.
Discussion and conclusion: asmathic disease appears to worst due to pregnancy, that is interrupted more often prematurely. The neonates are generally small for date; 2 cases of atopic desease, 2 of renal defects have been noticed. Our data confermed that fetal outcome from asthmatic pregnancy is different than from control group.

References:Huff R.W., Asthma in pregnancy, Med.Clin.N.Am.,73:653-660,1989

A.191

HELLP SYNDROME: CONSIDERATIONS ON 42 CASES

E.Gollo,R.Gasparini, S.Destefanis, M.Maresca
S. Anestesia e Rianimazione Ospedale S.Anna
Torino

Background & goal : Weinstein first, in 1982, gave the name of HELLP syndrome to a disease of pregnancy caracterized by hemolysis (H), elevated liver enzymes (EL) and low platelets (LP). This syndrome can appear before or after delivery often, not necessarly, associated with pregnancy induced hypertension. There is not uniformity about the criteria of definition, diagnosis, etiopathogenesis, epidemiology and therapy of the syndrome. Laboratory data that are generally used to define this desease are: bilirubinemia>1 mg%
AST,ALT > 100 UI/l, platelets < 150.000/mmc.
The incidence of preclampsia, eclampsia and HELLP syndrome, varies depending on the Authors from 2% to 12% . Maternal mortality observed is between 0 and 33%, perinatal between 10 and 60% . The main damage in the pregnant is the lesion of vascular arterial endotelium, caused by alternance of costriction and dilatation induced by hypertension.
Patients and methods: the study included 42 cases of HELLP syndrome treated in the years 1988-1993 (50.000 deliveries) at the S.Anna Hospital of Torino. The age of pregnant women included in the study was between 22 and 41 years. The diagnosis of HELLP syndrome was made on the basis of the following hematological findings:

- **bilirubinemia > 0,6 mg%**
- **serum epathic enzymes > 40 UI/l**
- **platelets < 150.000/mmc**

All subjects gave informed consent to the study. Ten patients, initially included in the study, were afterwards eliminated because they didn't satisfy previous criteria.
Anamnestic reports (age, obstetric history, familiar pregnancy induced hypertension, smoke, obesity, renal disease etc.) and laboratory data from blood exams before and during pregnancy have been settled to identifie markers predictive for the syndrome. Duration of pregnancy, modality of parturition, feto-maternal pathologies, mortality and follow up have been collected. Infant clinical data included gestational age, birth weight, Apgar score, percentyle and hematological data (platelets, red and white blood cell count, liver enzymes and bilirubin). All survived patients, with their children, have been contacted and submitted to clinical and laboratory valutations. The results are examined and discussed.

A.192

OUTPATIENT ANESTHESIA CONSULTATION AND EARLY DETECTION OF RISK FACTORS FOR DIFFICULT INTUBATION IN OBSTETRIC PATIENTS

Jamil Hamza, Xavier Dupont, Béatrice Ducot, Dan Benhamou
Dépt Anesthésie, Hôp St-Vincent-de-Paul, 75014 Paris, Hôp Béclère
92141 Clamart; Inserm U 292, Hôp Bicêtre, 94275 Bicêtre, France

Background and goal of study: Failed intubation is still the leading cause of anesthetic-related maternal mortality in obstetrics Risk factors for difficult endotracheal intubation have been recently studied in obstetrical patients (1) However, airway evaluation just before inducing anesthesia for emergency cesarean section does not allow a planned management of a difficult airway, such as early epidural anesthesia or fiberoptic intubation. Thus, the goal of this study was to systematically evaluate the airway of all the pregnant women during an outpatient anesthetic consultation in order to define which population of pregnant patients were at higher risk for potentially difficult airway (PDA)

Materials and methods: After institutional approval and over a 2 years period (1/01/89-30/12/90), all parturients who had attended our outpatient clinic during the last trimester of pregnancy participated to this study. The risk factors for PDA studied were the following: Mallampati class III, limited mouth opening, receding mandible and limited neck extension. The patients with at least one of these signs were considered to have a PDA. Demographic data (age, weight, height, body mass index (BMI) and medical problems (pregnancy-induced hypertension (PIH), diabetic) were noted. Patients who's BMI was over 30, were defined as obese. Patients with blood pressure over 140/90 mm Hg were defined as having PIH. The role of these demographic and medical data as risk factors associated with PDA were evaluated using multivariate analysis (logistic regression). $p<0.05$ was considered as statistically significant.

Results and Discussion: 3503 parturients (77.2 % of patients delivered during the study period) were included. 344 patients (9.8 %) had at least one sign of PDA. Both obesity and PIH were significant risk factors for difficult airway visibility (tables). In addition, parturients with PIH are at higher risk for emergency operative delivery. Early evaluation of these patient's airway in order to detect those with increased risk for poor airway visualisation may be particularly useful when an increased risk of cesarean section is anticipated. This allows a planned management including early epidural anesthesia to avoid the need for general anesthesia and all the technical supplies useful for a difficult intubation if general anesthesia becomes necessary in these patients.

Conclusion: Nearly 10% of obstetric patients have at least one sign of potentially difficult airway. Among these patients, those with PIH or obesity are at higher risk: a systematic early anesthesia consultation may be particularly beneficial in these patients.

References: Rocke DA et al Anesthesiology, 1992; 77: 67-73

Table 1: Factors associated with an increased risk of PDA

Factor (p value)	Odd Ratios Confidence interv
PIH p < 0,001	1,60 [1,16-2,20]
BMI > 30 p < 0,01	1,59 [1,17-2,15]

Table 2: Percentage of patients with at least one PDA factor

	NO PIH	PIH
BMI < 30	237/2793 8.5 %	39/257 15,2%
BMI > 30	47/320 14.7 %	21/133 15,8 %

A.193

PLACE OF BLEEDING TIME IN DIAGNOSIS OF HEMOSTATIC ABNORMALITY IN PREGNANCY.

Christophe Canevet, Gilles Theeten, Anne Sophie Ducloy-Bouthors
Renée Krivosic-Horber.

Department of anesthesiology I, Hôpital B
CHRU Lille, 59037 Lille cedex, France

Background and goal of study : during pregnancy, changes of the components of the hemostatic system are well known (1), but the diagnosis of high risk haemorrhagic modifications is not easily recognisable in emergency.

After defining the normal range of bleeding time (BT) during the third term of pregnancy, the respective use of oriented questionnaire, of BT and laboratory test (Platelet Count (PC), Prothrombin Time (PT), Partial Thromboplastin Time (PTT)) is evaluated.

Materials and methods : A BT was performed by one experienced examiner using IVY SIMPLATE II technic (normal range : 120-540 seconds) in 78 patients attending for a routine antenatal control. A detailed medical and obstetric history and a complete physical examination was obtained for all patients. A blood sample was drawn for PC, PT and PTT.

Results and discussion : The normal range of BT during the third term of pregnancy is 197-473 seconds (CI 95%). The mean BT is 335 ± 70 seconds (range, 180-480),

- 6 hemostatic abnormalities were detected : 2 gestationnal thrombocytopenia with normal BT and 4 prolonged BT.
- A BT must be performed as soon as an abnormality is detected by medical history or physical examination. In those six cases, questionnaire was positive.
- Laboratory tests (PC, PT, PTT) are useful to detect asymptomatic abnormalities.
- Prediction of hemostatic abnormalities is performed at 100% by oriented questionnaire.

Conclusion : Normal upper limit of BT during the third term of pregnancy is lower than in non pregnant patients.

- Hemostatic abnormalities can be predicted by oriented questionnaire, confirmed by laboratory test and/or BT.

Reference : 1. Conard J., Samama M.M. : Hémostase. In : *Pathologies maternelles et grossesse.* Ed. Medsi - Mc Graw-Hill, Paris, 1988 ; pp 571-587.

A.194

PREDICTION OF MATERNAL INFECTION BEFORE PERFORMING EPIDURAL ANALGESIA OF LABOR.

A.S. Ducloy, E. Buy, JC Ducloy, G. Theeten,
JC Monnier, R. Krivosic-Horber

Department of Anesthesiology, Hôpital B, CHRU Lille,
59037 Lille cedex, FRANCE

Background and goal of study : The risk of epidural abscess and or meningitis, following regional anesthesia, was not confirmed clearly in a febrile parturient (1,4,5). However one study concerning bacteriemic rats (2), suggest that bacteriemia may constitute a risk factor. Chestnut's advise (3) was to put in balance the risk of general anesthesia and the risk of meningitis while using epidural anesthesia.

However, to reach a decision, the anesthesiologist can be helped by some arguments to predict the existence of infected parturient before performing epidural anesthesia.

Material and methods : The prospective study include all 494 parturients during 3 months. 29 informations were noted : temperature, fetal tachycardia, shivering, epidural analgesia, duration of fasting and labor, number of obstetrical examinations, meconial amniotic fluid, urinary tract infection, premature rupture of membranes (PROM),use of intracervical prostaglandin. Maternal infection has been improved by bacteriologic cultures (blood, urine, amniotic fluid and neonate). Statistiq method was a logistic model of the best diagnostic elements selected by multivariate analysis step by step (SAS).

Results : Incidence of maternal infection during labor is 3,1 %.

The predictive elements of parturient's infection were determined by selecting variables which we dispose before performing epidural analgesia. Four predictive elements were determined with the respective odds ratio and frequencies (table 1) : foetal tachycardia : 26.9, urinary tract infection : 6.3, PROM : 3.9, Prolonged fasting : 5.2.

To discriminate maternel infection risk, if only one of these elements exist, the model has determined 3 predictives elements at the beginning of painfull labor : Hyperthermia or shivering or foetal tachycardia , meconial amniotic fluid, Dystocy .

Discussion and conclusion : The predictive elements selected before the set of epidural catheter (foetal tachycardia, urinary tract infection, PROM>24hours prolonged fasting) permit to define a group of risk. If foetal tachycardia or more than 2 signs exist, maternal infection is probable. If only one sign exist, the proposed attitude is to delay the set up of epidural catheter, and to wait for the active painfull labor. At this time, apparition of foetal tachycardia, shivering, hyperthermia and of meconial ammiotic fluid or dystocy, permit to confirm at 95 % the presence of maternel infection. Then, decision to set-up an epidural analgesia or not, will be more justifiable ; same reflexion will follow the use of antibiotics before the set-up of the epidural catheter.

Table 1 : frequencies of infection at T0

Predictive elements Infection	0	1	Tachycardie foetale and/or 2 or 3 elements
0	337	124	16
1	1	8	8

References: 1)Regional anesthesia, 1992:17:84-86, 2) Anesthesiology, 76:736-742, 1992, 3) Anesthesiology, 76:667-669, 1992, 4) Anesthesia 40:1219-1225, 1985, 5) Br J Anesth, 64:537-541, 1990

A.195

THE EFFECT OF ANAESTHETIC TECHNIQUES ON PERIPARTAL MATERNAL INTERLEUKIN-6 LEVELS.

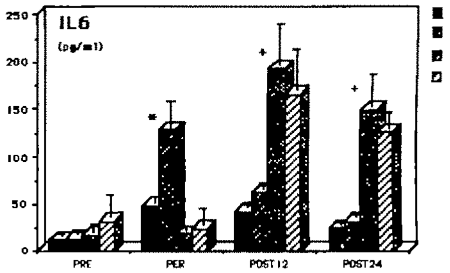
Raf De Jongh, Martine Puylaert, Willem Ombelet, Rene Heylen, Eugene Bosmans.

Departments of anaesthesia and gynaecology, Sint Jans-ziekenhuis, Genk, Belgium Eurogenetics Belgium

Background and goal : Cytokines participate in the physiology of normal and abnormal labour and cervical ripening Interleukin-6 (IL-6) is a sensitive, early and integral responder in the cascade of host mediators after injury. Its action is pleiotropic : it induces or inhibits proliferation or differentiation of several cells. The goal of this preliminary study was to evaluate the changes of peripartal maternal IL-6 levels, using different anaesthetic or obstetric techniques.

Material and methods : 20 patients received epidural analgesia on their request : top ups with bupivacain 0.125 % with adrenaline and sufentanyl (group epi). 20 patients had primary caesarian section under epidural anaesthesia with bupivacain, adrenaline and sufentanyl (group PCE) and 10 patients had section under general anaesthesia (group PSG) 31 patients without pain releif served as control (group cont). Venous blood was taken after hospital admission (pre), just after parturition (per), ± 12 hours postpartum (post12) and ± 24 hours postpartum (post24). ELISA was used to determine IL-6 serum levels.

Results and discussion : IL-6 increased after delivery with peak levels immediately after birth in patients with vaginal delivery and 12 hours postpartum in patients with caesarian section. In the group epi, IL-6 levels per and post12 were significantly higher compared to the levels of group cont. Stepwise regression showed that IL-6 levels after birth in patients with vaginal delivery correlated with the duration of labour and oxytocin administration, and with induction of labour. No IL-6 differences were found between patients of group PSE and PSG.



Conclusion : IL-6 levels after caesarian section are comparable with IL-6 levels after surgery with moderate stress or injury. IL-6 increases after vaginal delivery must be explained by labour and/or cervical ripening. Explanations for higher increases of IL-6 in patients receiving epidural analgesia remains speculative : bias, hormonal differences, higher stimulation with oxytocin, and prolonged labour.

References :Kelly R et al. Lancet 1992; 339: 776-777.
De M et al. Endocrinology 1992; 131: 14-20.
Cruickshank A et al. Clin Sci 1990; 79: 161-165.

A.196

IMPAIRED EFFICACY OF EPIDURAL ANALGESIA AND ANESTHESIA IN PARTURIENTS AFTER PREVIOUS DURAL PUNCTURE

Jean-Pierre Fulgencio, Jamil Hamza, Françoise Toubas.
Dépt d'Anesthésie, Hôpital St-Vincent-de-Paul, 75014 Paris, France.

Background and goal of study: Impaired epidural analgesia has been reported in patients who had had an inadvertent dural tap during a previous epidural catheter insertion (1). This occurred regardless of the need for a blood patch (1) and was solely related to the dural puncture itself. However, the effect of a previous diagnostic lumbar puncture on the epidural efficacy was unknown. The goal of this prospective study was to assess the effect of a previous dural puncture (DP), – whatever the reasons for it – on the efficacy of lumbar epidural analgesia or anesthesia (LEA) in obstetric patients.

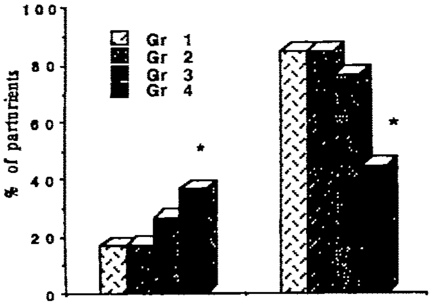
Materials and methods: After institutional approval and over a 9 months period (1/01/92-30/09/92), all term parturients who had attended our outpatient clinic during the third trimester of pregnancy and who required LEA during labor or delivery participated to this study. During the outpatient anesthesia consultation, patients were allocated to one of four groups: absence of previous LEA or DP (group 1), successful previous LEA without previous DP (group 2), impaired previous LEA without previous DP (group 3), previous DP either during LEA or for diagnostic lumbar puncture (group 4). All data related to LEA (difficulty and technical problems during catheter insertion) and the delivery period (mode of delivery) were noted. During the 5 first days postpartum, a questionnaire aimed at assessing the patient's feelings about their LEA was completed by the patients: global satisfaction and adequacy of pain relief were evaluated. Statistics of all collected data included either ANOVA for quantitative data or a Chi square test for qualitative data; $p<0.05$ was considered as statistically significant.

Results and Discussion: 1213 parturients were included. Technical problems related to epidural catheter insertion were more frequent in patients of group 4 than in the three other groups (figure). Good pain relief was achieved in only 44.4% of patients in group 4: this was significantly lower than in groups 1, 2, and 3 (figure). In agreement with a previous study on dural tap complicating a LEA (1), our study demonstrates that previous dural puncture, either diagnostic or inadvertent during LEA, is associated with an increased incidence of technical problems, inadequate analgesia and patient's dissatisfaction about LEA. Although our study can not explain the reasons of these results, we can speculate that fibrous sequelae of dural puncture may play a role in limiting the spread of local anesthetics injected in the epidural space and thus the efficacy of epidural analgesia.

Conclusion: Previous dural puncture increases the risk of inadequate epidural analgesia or anesthesia. The effects of previous spinal anesthesia with the new "atraumatic" needles deserve further attention.

References: (1) Ong BY et al, Anesth Analg 1990; 70: 76-79.

Figure: Percentage of parturients with technical problems and with good pain relief in each group.



* = p < 0.01

A.197

A COMPARISON OF THREE EPIDURAL INFUSION TECHNIQUES IN LABOUR

DG Wright, BVS Murthy, K Fitzpatrick, JPH Fee.

Departments of Anaesthetics Queen's University of Belfast & Belfast City Hospital, Northern Ireland.

Background and goal of study : Epidural fentanyl and alfentanil have both been used in combination with bupivacaine for the provision of analgesia in labour (1,2). The aim of this randomised, controlled study, was to compare the effectiveness of fentanyl and alfentanil when combined with bupivacaine for pain relief in labour.

Materials and methods : Fifty primagravidae in established labour, who had received no prior opioids, were given an initial bolus of 10 mls of epidural bupivacaine 0.375%, followed by a continuous epidural infusion of one of 3 test solutions, according to a double blind technique. The first test solution contained bupivacaine 0.1% only, whereas the second and third solutions contained in addition respectively, fentanyl 1ug/ml, and alfentanil 10ug/ml. The epidural solution was infused at 10-18 ml/hour, to maintain sensory blockade at T8. Increments of 4 ml bupivacaine 0.375% were given for breakthrough pain. Pain scores were assessed with 10cm visual analogue scales (VAS).

Results & discussion : Results are shown below, as mean and standard deviation.

	Bupivacaine only (n=17)	Bupivacaine fentanyl (n=16)	Bupivacain alfentanil (n=17)
Bupivacaine total dose	105.1 (37.8)	104.0 (20.0)	102.2 (30.1)
Total dose opioid (ug)	0	64.8 (20.7)	589.1 (265.1)
Topups	14 (0.95)	2 (0.34) *	6 (0.60)
Pain score	1.46 (1.04)	0.73(1.1)**	0.82(0.8)
Duration of epidural (minutes)	310.0 (175.1)	311.0 (112.9)	298.0 (134.5)

* $p<0.05$ compared to control (t-test)
** $p<0.05$ compared to control (Mann-Whitney U-test)

Significantly fewer topups were required in the fentanyl plus bupivacaine group, and pain scores were significantly lower than controls ($p<0.05$). In all groups bupivacaine doses, motor block, mode of delivery, duration of epidural analgesia, and neonatal Apgar scores were similar.

Conclusion : Epidural fentanyl in combination with bupivacaine afforded significant improvement in the quality and the continuity of epidural analgesia in labour, when compared to bupivacaine alone.

References : (1). Canadian Journal of Anaesthesia 1991; 38: 303-10.
(2). European Journal of Anaesthesiology 1993; 10: 183-7.

A.198

DOUBLE-BLIND COMPARISON OF OBSTETRICAL ANALGESIA WITH SUFENTANIL OR FENTANYL ASSOCIATED WITH 0.25% BUPIVACAINE

JC. Jorrot, MD., JD. Lirzin, MD., A. Ghimouz, MD., J. Coste MD., Ch Conseiller, MD.
Dept of Anesthesia University Paris V, Cochin Hospital
75014 -Paris -France

BACKGROUND & GOAL OF THE STUDY: Epidural narcotics are widely used in obstetric analgesia in combination with local anesthetics. However, the optimal dosage of epidural sufentanil is still controversial and its advantages over epidural fentanyl has not been extensively studied. Therefore, this study was performed to try to determine these issues.

MATERIALS & METHODS : After Institutional committee approval and informed maternal consent, 120 nullipara parturients requesting epidural analgesia in early labor were studied. The epidural space was cannulated at the L3-L4 interspace and a test dose of 0. 25% plain bupivacaine (4 ml) was injected through the catheter. There after, they were randomly allocated to receive either 20 mcg of sufentanil (group1), 25 mcg of sufentanil (group 2) or 75 mcg of fentanyl (group 3) administrated through the epidural catheter in a double manner. Five minutes later, all the patient had an epidural injection of 8 ml of 0. 25% plain bupivacaine. Troughout labor, on-demand analgesia was ensured by to-ups of 0. 25% plain bupivacaine.

We recorded the following data: time between epidural test dose and onset of analgesia. duration and quality of analgesia till the first epidural re-injection, side effects (such as pruritus), mode of delivrery and neonatal condition at birth. All results are expressed as mean ± SD. Statistical analysis was performed using analysis of variance followed by Fisher's exact test. $p < 0.05$ was considered significant.

RESULTS & DISCUSSION : There is no difference between the three groups regarding maternal characteristics, term, cervical dilatation and pain score before epidural analgesia.

Time to onset of analgesia is similar in the 3 groups. In group 1 and 2 when compared to group 3, duration of analgesia is significantly larger (141.7±6.7 min, 146.9±6.4 min, 109.9±6.3 min respectively) and quality of analgesia is better (table1).

Dizziness is more frequent in group 1 and 2 than in group 3, but prurit is more frequent in group 2 (table 1).Rate of delivrery and neonatal conditions are similar in the three groups.

Addition of epidural sufentanil 20 or 25 mcg to 0.25% plain bupivacaine induce a larger analgesia than to 75 mcg of epidural fentanyl. This result is in agreement with a previous study (1). However, we found that analgesia was also better with sufentanil 20 or 25 mcg than fentanyl 75 mcg in contrast with G. Phillips and our previous study results using 15 mcg of sufentanil (2).

CONCLUSION : We conclude than a dosage of 20 mcg of epidural sufentanil provide a larger and better analgesia than 75 mcg of epidural fentanyl, and may be the better dosage as it induces less pruritus than 25 mcg of epidural sufentanil..

Table 1: Quality of analgesia and maternal side Effects

	gr1 n = 37	gr2 n = 37	gr3 n = 34
VAS at 30min.	0.22 ± 0.09*	0.20 ± 0.09*	0.76 ± 0.25
Persisting painful aera	0*	0*	4
Unilateral block	0*	3*	6
Pruritus	12	23**	14
Dizziness	9*	7*	0

* $p < 0.05$ vs gr 3, ** $p < 0.05$ vs gr1 and gr 3

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A.199

TITLE: THE ELECTIVE USE OF OXYTOCIN INFUSION DURING LABOUR IN NULLIPAROUS WOMEN USING EPIDURAL ANALGESIA: A RANDOMISED DOUBLE BLIND PLACEBO CONTROLLED TRIAL.

AUTHORS: Shennan AH, Smith R, Browne D, Edmonds DK and Morgan B.
AFFILIATION: Queen Charlotte's and Chelsea Hospital, Goldhawk Road, London W6 OXG

BACKGROUND AND GOAL: The use of epidurals is accompanied by an increase in the operative delivery rate especially involving malposition of the fetal head.[1] A policy of active management of labour has clearly been shown to reduce the operative delivery rate[2], and recent evidence suggests this holds true in primiparae with epidural analgesia[3]. There is no published data concerning the elective use of oxytocin during the first stage of labour. We investigated what effect the elective use of oxytocin infusion in labour, on nulliparous women using epidural analgesia, had on obstetric outcome.

MATERIALS AND METHODS: 93 nulliparous women in a London Hospital, who had requested an epidural for pain relief in labour (≤6cm.), were given an intravenous infusion of oxytocin or placebo. An epidural was achieved with an initial dose of 15mls of 0.125% bupivicaine, followed by an infusion (0.125%) at 10mls per hour, with 15ml top ups if required.

RESULTS: When oxytocin was electively used there was a reduction in the length of the first stage of labour (696min. to 578min. p=<0.05) even though more than half of the control group (53%) required oxytocin augmentation. There was no significant difference between the number of operative deliveries (34 {76%} vs 35 {76%}). Over 90% of operative deliveries were for delay in the first or second stage of labour. The rotational delivery rate was less in the study group (2 {4%} vs 5 {11%}), though this did not reach significance. There were no adverse effects on the fetus, as judged by cord pH measurement, Apgar score, admission to the special care baby unit and neonatal jaundice.

CONCLUSION: The prophylactic use of oxytocin in nulliparous women with epidurals reduces the length of the first stage of labour and appears to be safe. It does not reduce the operative delivery rate, but may improve the rotational delivery rate.

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A.200

OXYTOCIN (O) CAUSES ST-SEGMENT DEPRESSION DURING CAESAREAN SECTION - A DOUBLE BLIND COMPARISION WITH METHYLERGOMETRINE (M).

M Svanström, G Johansson, E Bålfors.

From the Department of Anaesthesia, University of Umeå, Umeå, Sweden.

Background & goal of study: ECG ST-segment depression is common in healthy women undergoing CS. Its cause and clinical significance remain speculative (1, 2). Preliminary data have shown a time-effect relationship between iv O and hypotension, tachycardia and transient ST-segment depression of short duration (3). The present study evaluates the influence of O versus M on haemodynamics and on the incidence of new ECG ST-segment depression according to a blinded, randomized, partial cross-over study design.

Patients & methods: 20 healthy women were studied while undergoing elective CS under spinal/epidural anaesthesia. Radial artery pressure, the V1-V6 leads of a 12-lead ECG and the change in spatial ST vector magnitude (STC-VM) by vectorcardiography (VCG) were recorded continuously. Heart rate was derived from the ECG. ST-depression were measured 60 msec after the J-point and regarded significant if horizontal or downsloping and ≥ 0.1 mV. STC-VM≥ 50 μV was regarded as abnormal. STC-VM was plotted vs pressure rate ratio (P/R - mean arterial pressure/heart rate) to study the role of haemodynamic changes. Left lateral tilt was maintained until delivery and iv ephedrine given as needed to keep systolic blood pressure above 95 mmHg. Immediately after delivery, 10 IU of O (n=10) or 0,2 mg of M (n=10) was given blindly iv. If clinically indicated, a second open dose of oxytocic (5-10 IU of O) was injected iv.

Results: O produced a short lasting significant change of STC-VM ($55 \pm 57 \mu$V, range -3 to 178μV, p=0.004) peaking after 30-120 sec. In one patient with marked ST-segment depression in the scalar chest leads, ventricular dysrhytmias precluded the automated VCG analysis. STC-VM exceeded 50μV in 5/9 and correlated closely and inversely with P/R (r=-0.963, p=0.000, n=9). The sum of ST-segment depression in the six chest leads correlated with STC-VM (r=0.879, p=0.002, n=9). All haemodynamic aberrations and ST-segment changes were normalised within 180 sec. M produced marginal, but significant increase of P/R (p=0.041) and 1/10 had significant ST-segment depression (p=0.027 vs O). There was no correlation between STC-VM and P/R. Reinjection of O produced significant ST-segment depression in 5/8 women previously given M (STC-VM range 55-114 μV) but in 0/4 previously given O.

Discussion & conclusions: Our results show that O produces ST-segment depression in women undergoing CS, the magnitude of which is closely and linearly related to a fall in P/R. The pattern of pathological ST-segments, the spatial directional ST-vector changes, the onset of severe ventricular dysrhytmias accompanying ST-segment depression in one patient and the low levels of P/R during maximal ECG/VCG changes indicate that ischaemia should be suspected.

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A.201

TITLE: COMBINED SPINAL EPIDURAL ANESTHESIA FOR CAESAREAN SECTION USING THE NEEDLE THROUGH NEEDLE TECHNIQUE: EFFECTS OF SUBCUTANEOUS OR EPIDURAL BUPRENORPHINE (Bu) FOR PROLONGATION OF POSTOPERATIVE ANALGESIA.

AUTHORS: E.WYSS,M.D., P.MONS, M.D., J.M.TEISSIER, M.D.,
J.L.GUILLAUME,M.D.,B.PIERROT, M.D.

AFFILIATION: Department of anesthesiology.
Manchester Hospital. Charleville-Mezieres.
08011.FRANCE

INTRODUCTION: Epidural Bu has been described for the treatment of acute postoperative pain (1). Bu has been also used subcutaneously (2). We compared in a double blind fashion the effects of subcutaneous or epidural Bu on the duration of analgesia after combined spinal epidural anesthesia for caesarean section using the needle through needle technique. Our aim was to seek a simple and safety method of postoperative pain control that provided adequate analgesia.

METHODS: After informed consent and institutionnal approval, 60 ASA I female undergoing caesarean section were assigned to one of two groups of 30 patients each. The epidural space was identified using the loss resistance technique (Tuohy 18G). The spinal needle was advanced until the tip was felt to puncture the dura (Quincke 27G, 11.9 cm). After appearance of CSF 0.09mg/cm 0.5% Bupivacaine was injected. In addition group A received 5ml chloride saline (CS) in the epidural space and 0.3mg Bu subcutaneously, Group B 0.3mg Bu added to 4 ml preservative free (CS) in the epidural space and 1ml (CS) subcutaneous. Duration of analgesia was determined by the patient's first request for analgesics (acetaminophen 1gr) in the two groups. The quality of analgesia was assessed by VAS within the 24 hours. Statistical analysis was done with ANOVA for each data.

RESULTS: Analgesia was achieved as early as the 5th minute in the two groups. No problem occured during the surgical procedure. Analgesia was significantly prolonged in group B (589±297mn) compared to group A (195±148mn) ($p<0.001$). The request for supplementary analgesia was significantly lower in group B (acetaminophen 1gr) compared to group A (acetaminophen 3gr). Overall pain was significantly lower in group B wharas maximum pain usually due to uterus contraction after delivery was the same in the two groups. No serious side effect was observed in the post operative period for women or child. 5% of the patient suffered from post dural puncture headache requiring a blood patch, effective in all cases. There were no nausea or vomiting in both groups.

DISCUSSION: In our study epidural Bu. significantly increases duration of sensory block after caesarean section and decreases the request for supplementary analgesia without side effects. It seems that epidural Bu when using combined spinal epidural anesthesia is a simple and safe method for postoperative analgesia.

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A.202

SEQUENTIAL SPINAL-EPIDURAL BLOCK FOR ELECTIVE CESAREAN SECTION. EFFICACY OF SUBARACHNOIDAL SUFENTANIL

M.Möllmann, H. J. Lübbesmeyer, D. Holst, L. Fanard, A.Van Steenberge

Klinik und Poliklinik für Anästhesiologie
und operative Intensivmedizin,
Westfälische Wilhelms-Universität,
Münster, Germany and
St. Anna Kliniek, Brussels, Belgium

The efficacy and safety of sequential spinal (29 gauge needle) and epidural anesthesia for elective cesarean section[1] was evaluated in two groups of parturients:

Group I (n=26) received 1.8 to 2.0 mL (dependent on the height of the patient) plain bupivacaine (BV) 0.5%;
Group II (n=26):1.8 to 2.0 mL BV 0.5% (+1/200,000 epinephrine) plus $5\mu g$ (1mL) sufentanil subarachnoidal.

No significant differences in onset of analgesia, spread of sensoric or motoric blockade or hemodynamic changes could be observed. Hypotension, (systolic blood pressure < 100 mmHg) requiring pharmacologic intervention, occurred in 8 and 9 patients in group I and II, respectively. Overall occurrence of visceral pain was low (6.5%) in group I and none in group II (+spinal sufentanil + epinephrine). No post dural puncture headache was observed.

Addition of $5\ \mu g$ of sufentanil and $10\ \mu g$ epinephrine subarachnoidal improved analgesia without side effects. The sequential spinal epidural anesthesia combines the versatility of spinal with the variability of epidural anesthesia.

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A.203

EFFECT OF THE ADDITION OF INTRATHECAL MORPHINE ON THE EXTENT AND QUALITY OF SPINAL ANALGESIA PRODUCED BY BUPIVACAINE

DT Knights, ID Smith, D Bogod.
Department of Anaesthesia, City Hospital, Nottingham, U.K.

Background: The effect of intrathecal morphine on the extent and quality of block produced by hyperbaric bupivacaine has been studied but the results are variable[1,2]. Dilution of local anaesthetic solution may decrease the quality of the block or the increased volume may lead to greater spread. This has been studied[3] but not using a standard technique for spinal analgesia. We therefore aimed to study these aspects of spinal analgesia and to assess the postoperative analgesia produced.

Materials and Methods: 60 patients scheduled for elective caesarean section under spinal anaesthesia were randomly allocated to one of three groups;

Group 1. 2.5ml 0.5% heavy bupivacaine.
Group 2. 2.5ml 0.5% heavy bupivacaine + 1ml 0.9% saline
Group 3. 2.5ml 0.5% heavy bupivacaine + 0.2mg morphine.

A standard spinal technique was used in all cases. All further clinical management was undertaken by a second anaesthetist who was unaware of the injectate given. Loss of temperature perception was used as the indicator of block height. Patients were asked to mark visual analogue scales (VAS) of pain after peritoneal opening, in the recovery unit (in respect of the whole operation) and 24 h postoperatively (in respect of worst pain since leaving the recovery unit). All patients received diclofenac 100mg PR at the end of surgery and 18h later. Patients not receiving intrathecal morphine could have intramuscular morphine 0.15mg.kg^{-1} on request.

Results and Discussion: The results from one patient were excluded as the protocol was not followed. No patient required supplemental analgesia intraoperatively and there were no statistical differences in the incidences of intraoperative hypotension (17/59), nausea (18/59) or vomiting (7/59) or in the dose of ephedrine required. There was no statistical difference between the groups with respect to block height at any time. This confirms that the final extent of block is influenced more by the dose of local anaesthetic drug than the volume. VAS scores at peritoneal opening and in the recovery unit were not significantly different; this is consistent with intrathecal morphine having an onset time of 20-30 min. VAS scores at 24 h were significantly lower in Group 3 compared to Group 1 ($p<0.05$) and Group 2 ($p<0.05$).

Conclusions: The addition of intrathecal morphine 0.2mg to hyperbaric bupivacaine for production of spinal analgesia for elective caesarean section does not appear to alter the extent or quality of the block produced in the intraoperative period but gives improved analgesia postoperatively when compared to 'on request' intramuscular morphine.

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A.204

THE ADDITION OF CLONIDINE TO EPIDURAL MORPHINE PROLONGS POSTOPERATIVE ANALGESIA AFTER CESAREAN SECTION.

Celleno D and Capogna G
Department of Anesthesiology
Fatebenefratelli General Hospital
Rome, Italy

Introduction: Epidural clonidine (400-800 mcg) after cesarean section produced complete analgesia of 4-5 h duration, accompained by side effects such as sedation, prolongation of epidural anesthesia and bradycardia (1). The addition of 150 mcg of clonidine prolonged postoperative analgesia in non obstetric patients (2). In this randomized double-blind preliminary study, we evaluated the effects of the addition of clonidine to epidural morphine on duration of postoperative analgesia in cesarean section patients.

Methods: Thirty patients undergoing elective cesarean section with epidural anesthesia (lidocaine 2% with epinephrine 1:200.000) were divided to receive epidurally, at the end of surgery, a mixture of 10 ml of solution containing 2 mg of morphine diluted with 0.125% bupivacaine with or without 75 mcg of clonidine. Duration of analgesia, assessed as pain-free interval (first analgesic request) and occurrence of side effects were noted.

Results: Results are reported in the Table. None of the patients reported hypotension or bradycardia. Two patients of clonidine group reported drowsiness.

Table 1:Duration of Postoperative Analgesia (hours)

	mean	sd	mse
morphine	6.11	1.38	0.34
morph+clonidine	14.13	6.09	1.57

(P<0.0001 CI 95%: 4.9/11.5)

Discussion: This preliminary study suggests that the addition of clonidine to morphine doubles the duration of postoperative analgesia in cesarean section patients. Further evaluation on the effects on total postoperative consumption of morphine and a dose-response study are in progress.

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A.205

DURATION OF ANALGESIA FOLLOWING CAESAREAN SECTION UNDER SPINAL ANAESTHESIA - THE EFFECT OF SPINAL MORPHINE AND RECTAL SODIUM DICLOFENAC.

M.J. ROONEY, A.R. DENNIS, M.F. REID AND D. BOGOD.
DEPT. OF ANAESTHESIA, QUEENS MEDICAL CENTRE, NOTTINGHAM, UK.

Background: Intrathecal morphine produces prolonged post-operative analgesia [1]. Non-steroidal anti-inflammatory drugs supplement analgesia [2]. We have studied the effect of spinal morphine and rectal diclofenac on the duration of initial analgesia following Caesarian section under spinal anaesthesia.

Patients and methods: The analgesic requirements of 139 patients who received spinal anaesthesia for elective Caesarean section were studied retrospectively. The patients were divided into 4 groups. All patients received a spinal anaesthetic consisting of 2.5 - 3 ml of 0.5%. bupivacaine. Group 1 received no extra analgesia at the time of operation. Group 2 received rectal diclofenac 100mg in recovery. Group 3 received intrathecal morphine 0.2mg. Group 4 received both intrathecal morphine 0.2mg and rectal diclofenac 100mg. The duration of analgesia was measured as the interval between the spinal injection and the first request for postoperative analgesia. 95% confidence intervals were calculated for the duration of analgesia in each of the four groups.

Results: Weight and age were similar in all groups. The mean duration of analgesia in each of the four groups was as follows: Group 1 2.6 hours (CI 2.3 - 2.9), Group 2 4.8 hours (CI 1.4 - 7.4), group 3 14.6 hours (CI 11.8 - 17.5) and group 4 20.2 hours (CI 18.0 - 22.3). It appears that in the patients receiving spinal morphine, rectal diclofenac given in recovery prevents the early moderate pain that often occurs.

Conclusion: The addition of rectal diclofenac to intrathecal morphine significantly prolongs the duration of analgesia following Caesarean section.

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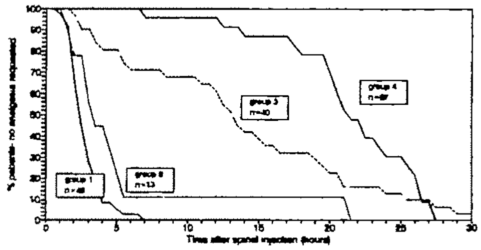

A.206

CONTINUOUS EPIDURAL INFUSION OF SUFENTANIL AFTER CAESAREAN SECTION : CONCENTRATION IN BREAST MILK

A. AUSSEUR*, G. THEETEN*, J.C. LEVRON**, R. KRIVOSIC-HORBER*
*: Department of Anaesthesiology I. Hospital B.
CHRU Lille France
**: Janssen Research Foundation - Val-de-Reuil. France

The aim of the study was to measure the concentration of sufentanil in human colostrum during epidural continuous administration in the first postoperative day.

Materials and methods : parturients at term were scheduled to undergo elective caesarean delivery under epidural anaesthesia by 2% lidocaine with epinephrine followed by 0,5% bupivacaine; after delivery, as early as pain was felt (T0), patients received one bolus of 10 mcg of sufentanil in 10 ml of isotonic saline serum followed by a 5 mcg per hour (1 mcg/ml) continuous infusion during the first postoperative day. Just before the first feeding time, maternal blood and colostrum samples were withdrawn to be analysed by radio immunoassay. Maternal respiratory rate and peripheral oxygen saturation by pulse oxymetry were noted.

Results : colostrum and serum concentration (ng/ml) :

	time of collection (hours)	colostrum	serum
Patient N°1	T0 + 8H	0,193	0,106
Patient N°2	T0 + 3H	≤ 0,02	0,08
Patient N°3	T0 + 7H	0,08	≤ 0,02
Patient N°4	T0 + 1H	≤ 0,02	≤ 0,02
Patient N°5	T0 + 4H	0,08	≤ 0,02
Patient N°6	T0 + 4H	≤ 0,02	≤ 0,02
Patient N°7	T0 + 5H	0,06	0,12

No respiratory depression occurred; the only side effect was a high incidence of pruritus but all patients wished the same analgesia for a new caesarean.

Discussion : like intravenous fentanyl (1) or epidural morphine (2), sufentanil appears in colostrum up to a milk/serum ratio greater than one ; with those small concentrations (compared with mean serum concentrations after continuous intravenous infusion : 0,4 to 0,7 ng/ml) and because of the bad oral bioavailability of opiates, we conclude that 5 mcg/hour continuous epidural sufentanil analgesia may be used safely in breast feeding women.

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A.207

COMPARISON BETWEEN TWO TECHNICS OF HEMODYNAMIC EVALUATION IN THE ICU : A PROSPECTIVE STUDY

D. Eyraud, R. Bourlier, J. P. Goarin, B. Vivien,
M. Saada, J. J. Rouby, P. Viars.
Department of Anesthesiology, Hospital of La Pitié,
University Paris VI, France.

Aim of the study : Right heart catheterization is commonly used in ICU to evaluate the hemodynamic status of unstable patients. Recently, transesophageal echocardiography (TEE) has been introduced in the ICU for the same purpose. Thus, we compared both technics for assessment of hemodynamically unstable patients.

Patients and methods : 46 adults admitted in the ICU were prospectively included. Mean arterial pressure was invasively measured. Pulmonary arterial and capillary wedge pressures, systemic vascular resistance and cardiac output were obtained using a Swan-ganz catheter. TEE evaluation of preload was derived from end-diastolic area and left ventricular function (LVF) was derived from LV ejection fraction. Right heart catheterism (RHC) and TEE were performed and analysed by 2 different highly-trained experts blinded from each other. The following hemodynamic diagnosis could be made : 1) hypovolemia or normovolemia, 2) decreased or normal LVF.

Results : evaluation of the 2 parameters was possible in all patients. Concerning volemia, RHC and TEE were in agreement in 31/46 patients (table 1). Concerning LV function, RHC and TEE were in agreement in 36/46 patients (table 2). In 20 patients, TEE provided new diagnostic elements : segmental wall motion abnormalities (n = 11), severe valvular dysfunction (n = 4), severe pleural effusion (n = 4), right ventricular pseudoanevrysm (n = 1). Conversely in all patients, RHC provided accurate measurements of cardiac filling pressures and pulmonary shunt.

Conclusion : this study demonstrates a discrepancy between the two technics in almost 30 percents for volemia and more than 20 percents for LVF. Theremore they are completary : TEE brings anatomic result for volemic status LVF and additional diagnostic elements, whereas RHC allows a continuous measurement of cardiac pressures and an evaluation of pulmonary shunt.

Table 1 : Volemia

RHC TEE	normal	low
normal	20	7
low	8	11

Table 2 : LVF

RHC TEE	normal	disturbed
normal	16	5
disturbed	5	20

A.208

ASSESSMENT OF LEFT VENTRICULAR FUNCTION DURING APNEA TESTING FOR BRAIN DEATH.

Catoire P, Orliaguet G, Liu N, Beydon L, Bonnet F
Réanimation chirurgicale, Hôpital Henri Mondor, 94010
Créteil, FRANCE.

Background and goal of the study:
In France, apnea testing for brain death diagnosis is recommended to last at least 10 minutes (1).The goal of the test is to increase the PaCO2 up to 50 or 60 mmHg in order to check for the absence of respiratory centers activity. The effects of hypercapnia on left ventricular function (LVF) during the test are controversial (2). The goal of this study was to prospectively assess the effect of a greater than 10 minutes apnea testing on blood gas exchange and LVF.

Materials and Methods :
Seventeen consecutive patients clinically suspected of brain death, hemodynamically stable, with electrocerebral silence on two consecutive EEGs, and considered as potential organ donnors were studied. LVF was evaluated using transesophageal echocardiography with a CFM 750 (Diasonic ®) connected to a 5 MHz transesophageal probe. After a complete examination, the probe was let in the short axis position during apnea testing. The apnea testing was performed after obtention of a PaCO2 > 35 mmHg and 20 minutes of FIO2 1 ventilation. Heart rate (HR), mean arterial pressure (MAP), left ventricle end diastolic and systolic surfaces (LVEDS, LVESS), LVF assessed by fractionnal area changes (FAC), systolic wall motion (SWM) score, and blood gas were recorded before (control), and after 10 and 20 minutes of apnea testing.

Results were compared by ANOVA and Fisher's test.

Results and discussion:
HR, LVEDS, LVESS, SWM were not significantly changed during the study. The other results are reported on table 1 ·

	control	10 min apnea	20 min apnea
pH (iu)	7.41 ± 0.07	7.22 ± 0.05**	7.09 ± 0.08**
Pa02 (mmHg)	386 ± 99	309 ± 120**	276 ± 117**
PaCO2 (mmHg)	40 ± 3	70 ± 6**	95 ± 11**
MAP (mmHg)	75 ± 10	68 ± 13*	63 ± 11*
FAC (%)	47 ± 11	46 ± 14	52 ± 11*

*p < 0.05 versus control ; ** p < 0.01 versus control

Despite severe respiratory acidosis the increase in FAC suggests that apnea testing is hemodynamically well tolerated.

Conversely, the PaO2 decrease might result from absorption atelectasia due to FIO2 1 ventilation, which could be possibly detrimental in case of pulmonary transplantation.

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A.209

Slow arterial pressure oscillations during brain death

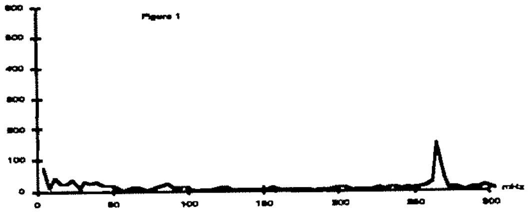
A. Descorps Declère, C. Baujard, B. Vigué, J. Duranteau, K. Samii.

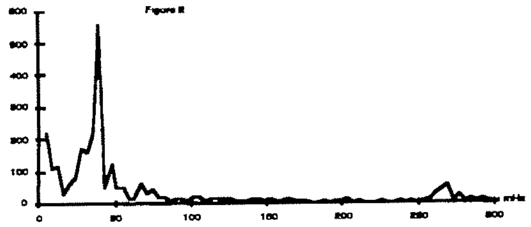
Réanimation Chirurgicale, Hôpital de Bicêtre, F 94275, le Kremlin Bicêtre, FRANCE

Background and goal of the study :
Spontaneous fluctuations of arterial pressure are cyclic. Slow fluctuations occurring at a rate of 0.04 - 0.13 Hz (Mayer waves) are considered as a reliable indice of sympathetic tone (1). Brain death is frequently associated to hypotension and decreased systemic vascular resistance which may be in part due to a decreased sympathetic tone. However the sympathetic system, during brain death has never been evaluated.

Materials and methods :
The short term variability of systolic arterial pressure was assessed in 7 patients in brain death using a computerised System (Labview Inforep* software). Frequency and amplitude of the oscillatory component were obtained by the fast Fourier transform algorithm.

Results and discussion :
The low frequency fluctuations of systolic arterial pressure was absent in 5 patients (figure 1) and present in 2 patients (figure 2) during the first measurement.
The second measurement performed one hour later showed the absence of low frequency component in all the patients.





Conclusion :
We conclude that the Mayer wave which is an indice of sympathetic activity disappear during brain death. However in some case, the criteria of brain death may preceede this autonomic abnormality.

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A.210

PERCUTANEOUS TRACHEOSTOMY USING BRONCHOSCOPIC CONTROL AND HFJV.

M.J. Van Boven , P. Pendeville and M. Hamoir .

Departments of Anesthesiology and Otorhinolaryngology.
UCL Medical School, St Luc Hospital,
1200 Brussels, Belgium.

Percutaneous tracheostomy by dilatation is a simple and quick method for placing a tracheal canula [1].It has been disparaged by some clinicians due to its blind nature.
In order to enhance safety, endoscopic control of the procedure with a flexible fiberscope has been proposed [2].
We describe our experience with a modified endoscopic technique using a rigid bronchoscope and high frequency jet ventilation (HFJV). This allows a permanent control of the tracheostomy procedure until the cannula has been installed.

Patients and method.Fifty percutaneous tracheostomies have been carried out between july 1992 and july 1993 using the Ciaglia percutaneous tracheostomy introducer set (Cook®).With the exception of two patients in which tracheostomy was carried out following diagnostic endoscopy, all the tracheostomies were performed in intensive care patients in which long intubation was intended.All the patients were mechanically ventilated and anesthetized by total intravenous anesthesia. The endotracheal tube was removed and replaced by a rigid bronchoscope (Sharplan ® L0210). Ventilation of the patients was achieved through the lateral arm of the bronchoscope using HFJV. The anesthesiologist could permanently control through the open bronchoscope the tracheal puncture and the successive introductions of the dilators and the tracheal canula.

Discussion.The subcricoid percutaneous tracheostomy technique by dilatation was described for the first time in 1985 by Ciaglia. It is not recommended in case of emergency, in children and when the cricoid cartilage cannot be easily identified. It has been strongly criticized given to the blind nature of the procedure and the possibility of false passage [3].Using a rigid bronchoscope instead of the endotracheal tube allows the anesthesiologist to control permanently the procedure. Moreover, HFJV allows to ventilate the patient in very safe conditions without having to obturate the proximal extremity of the bronchoscope; if blood and debris are projected in the trachea , direct aspiration can be carried out through the lumen of the bronchoscope. The technique is however limited since the uncuffed bronchoscope does not ensure a perfect tight seal of the trachea. It seems to us also contraindicated when difficult intubation is planned or in cases of cervical spine instabillity. Furthermore, the high frequency ventilation technique is difficult to apply when pulmonary compliance is low.

Conclusion. We propose a technique which allows a permanent visual control of the percutaneous tracheostomy procedure. This technique is limited in case of difficult intubation and when HFJV is contraindicated.

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2- Ann Thorc Surg 1989; 47: 314-315.
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A.211

RENAL EFFECTS OF LOW DOSE DOPAMINE INFUSION IN PATIENTS WITH SEPSIS SYNDROME.

Thierry Lherm, Gilles Troché, Nadia Gharsallah,
Jean-Fabien Zazzo, Dan Benhamou

Département d'Anesthésie-Réanimation. Université Paris-Sud, Hôpital Antoine Béclère, 92140 Clamart- FRANCE

Background and goal of study: Low dose (1-3γ/kg/min) infusion of dopamine (DA) is widely used in intensive care units to improve renal function. Experimental studies have shown that renal action of DA is related to activation of dopaminergic receptors (1). However, little is known about the clinical application of renal dose of DA. This study evaluates the renal effects of short and long term infusion of low dose of DA in severe septic patients.
Materials and methods: Patients were included if they had 1- a sepsis syndrome as defined by Bone (2) and 2- clinical signs of sodium and water retention (oedema or weight gain) and 3- not received neither diuretics within 8 hours nor DA within 24 hours before the beginning of the study. Two periods of 2 hours each were achieved on the first day (baseline-D_0, DA-D_0), and after 48 hours of infusion (DA-D_2, baseline-D_2) of 2γ/kg/min of DA. Hemodynamic (HR, MAP, MPAP, PCWP, CVP, CO) and renal parameters (urinary output, natriuresis and creatinine clearance) were collected at the end of each period. Wilcoxon signed rank test was used for statistical comparison and $p < 0.05$ was considered significant.
Results: On D_0 (n=20), urinary output, sodium excretion and creatinine clearance all increased by 100 % with DA (m ± sem). Hemodynamic parameters remained esentially unchanged. After 48 hours of DA infusion (n=14), the urinary output was still significantly increased as compared with baseline but the renal response to DA was significantly less than on D_0 ($p<.01$).
Conclusions: Dopamine has direct renal effect (without change in systemic hemodynamics) in patients with sepsis syndrome. However, the observed decrease in the renal effect of dopamine with time might be related to a "down regulation" of the renal dopaminergic receptors.
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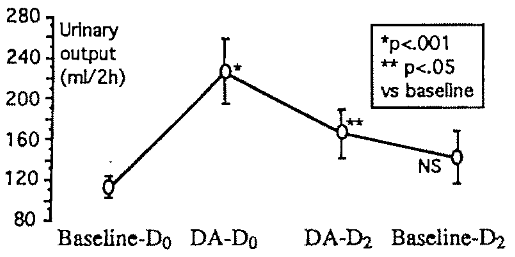
2-BONE RC et al: Crit Care Med 1989;17:389-393



A.212

RENAL EFFECTS OF LOW DOSE DOPAMINE IN PATIENTS WITH SEPTIC SHOCK TREATED WITH NOREPINEPHRINE.

Thierry Lherm, Gilles Troché, Andréa Passard,
Jean-Fabien Zazzo, Dan Benhamou.

Département d'Anesthésie-Réanimation, Université Paris-Sud, Hôpital Antoine Béclère, 92140 -Clamart- FRANCE

Background and goal of the study: Experimental studies have suggested an improvement of renal hemodynamics with low dose dopamine (DA) in animals either with septic shock (1) or treated with norepinephrine (2). However, the effect on renal function was not examined in these reports and no previous study has assessed the renal effects of low dose infusion of DA in patients with septic shock treated with catecholamines.
Materials and methods: Patients with septic shock were included if they: 1- were treated with catecholamines (norepinephrine and/or epinephrine, 2- had hemodynamic stability during at least 4 hours before measurements and had clinical signs of sodium and water retention (oedema or weight gain), 3- had not received neither diuretics within 8 hours nor DA within 24 hours. Two periods of 2 hours each were achieved: baseline and DA (2γ/kg/min). Hemodynamics (HR, MAP, MPAP, PCWP, CVP, CO) and renal parameters (diuresis, sodium excretion and creatinine clearance) were collected at the end of each period. Wilcoxon signed rank test was used for statistical comparison and $p < 0.05$ was considered significant.
Results and discussion: 13 patients were included in this study. Diuresis, sodium excretion and creatinine clearance were not significantly different during baseline and DA infusion periods. Systemic hemodynamic parameters were not modified during DA infusion.
Conclusions: This is the first clinical study to assess the effect of low dose dopamine infusion in patients with septic shock treated with norepinephrine and/or epinephrine. 2γ/kg/min of DA infusion does not improve renal function and systemic hemodynamics. This might be related to heterologous desensitization of dopaminergic receptors by prior infusion of catecholamines.
References:

(1) FINK MP et al: J Surg Res 1985; 38: 582-591.
(2) SCHAER GL et al: Crit Care Med 1985; 13: 492-496.

Parameters mean ± sd	Baseline	Dopamine	Stat
Diuresis (ml/2h)	206 ± 138	190 ± 112	NS
Na Excretion (mEq/2h)	10.9 ± 4.9	10.7 ± 4,1	NS
Creat Clearance (ml/min)	56.6 ± 51	52.4 ± 34	NS
HR (b/min)	99 ± 18	105 ± 17	NS
MAP (mmHg)	80.1 ± 10.5	74.6 ± 10.4	NS
PCWP (mmHg)	12.9 ± 5.9	13.4 ± 5.3	NS
CVP (mmHg)	10.2 ± 4.8	10.9 ± 4.9	NS
CO (l/min)	7.57 ± 2.4	8.36 ± 2.5	NS

A.213

ARDS EVOLUTION DURING THERAPEUTIC OPTIMIZATION LEADS TO ECCO2R-LFPPV INDICATION.

D Payen, N Guinard, C Gatecel, J Mateo, Intensive Care Unit, Lariboisiere University Hospital, 75010 Paris, France.

Extracorporeal CO_2 Removal with apneic ventilation ($ECCO_2R$-LFPPV) has been proposed as an alternative technique to conventional mechanical ventilation in severe ARDS. Since the indication is difficult to establish, its evaluation is still open to controversy. The aim of this study was to evaluate the decision making strategy used in our institution.

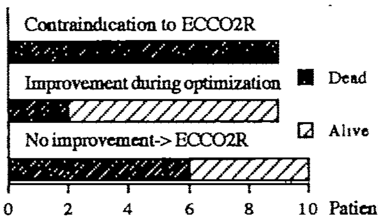
Methods: 28 patients (pts) suffered from severe ARDS were included (Lung Injury Score > 2.5 - 3.4±0.4, PaO_2/FiO_2 80 ± 32 mmHg, lung compliance < 30 ml/cmH_2O). All of them had the criteria of ECMO study. The decision making strategy was:

1) search for contraindications to ECCO2R: central nervous system disorders, hemorragic risk lesion, refractory shock, "chronic" multiple organ failure, major burns, chronic systemic disease;

2) therapeutic optimization: CTScan, drainage of pleural effusions, changes in ventilatory mode, improvement of VA/Q matching, negative fluid balance, attempt to improve organ failure;

3) patients improved during optimization were maintained on conventional ventilation; patients not improved during optimization were treated by $ECCO_2R$-LFPPV.

Results & discussion: pts distribution and mortality:



Initial gravity criteria were similar in the three groups and failed to make a decision for $ECCO_2R$. Only the therapeutic optimization allows to decide to keep on conventionnal treatment or to put on $ECCO_2R$-LFPPV.

A.214

PLATELET AGGREGATION, VON WILLEBRAND FACTOR ANTIGEN AND ACTIVITY, AND INHALED NITRIC OXYDE (NO) IN ARDS PATIENTS

ChM Samama[1], S Dreux[2], D Eyraud[1], R Bourlier[1], M Arock[2], Th Lecompte[3], JF Caussinus[4], L Puybasset[1], JJ Rouby,[1] P Viars [1] 1: Dpt. Anesth.-Réanim.-2: Labo. Urgences, GH Pitié-Salpêtrière, 3: Labo. Hémato. Hotel-Dieu, Paris - 4: Helena-France

Pulmonary arterial thrombosis is often observed during ARDS, and could be partially limited by NO-induced platelet aggregation inhibition. A prospective study was conducted to measure ex-vivo the effect of inhaled NO on platelet aggregation and von Willebrand factor antigen (vWF Ag) and activity (vWF RCo) in blood withdrawn from pulmonary and radial arteries. Methods: Six ARDS patients under mechanical ventilation, monitored by a Swan-Ganz catheter were included. Immediately before and one hour after NO administration (CFPO - 2 ppm), blood was sampled (citrated tubes) in the pulmonary and radial arteries. Platelet aggregation (Helena Packs 4®) was induced by ADP(5µM), collagen(10 µg/ml), ristocetin (1,5 mg/ml). Maximal intensity and slope were recorded. vWF Ag (Stago®) and vWF RCo (Helena-Packs 4®) were measured . Statistical analysis : ANOVA.

Results : No statistical difference was observed before and after NO administration. In addition, platelet aggregation and vWF Ag and activity did not differ between pulmonary and radial artery.

	ADP (% max)	collag (% max)	risto. (% max)	ADP (slope)	collag. (slope)	vWF Ag(%)
artery	48±12	87±16	80±13	56±31	65±23	210±26
artery NO	36±14	82±16	71±34	49±27	53±26	196±60
PA	39±12	81±15	71±13	45±24	54±25	243±10
PA NO	39±16	78±15	76±23	51±28	57±26	230±34

Discussion : No measurable effect was observed in this preliminary study when NO was administred at a 2 ppm concentration which induced significant beneficial effects on pulmonary vascular resistance and arterial oxygenation. Rapid fixation of NO on haemoglobin may explain the lack of detectable systemic effect, and, therefore a local antithrombotic effect cannot be excluded.

A.215

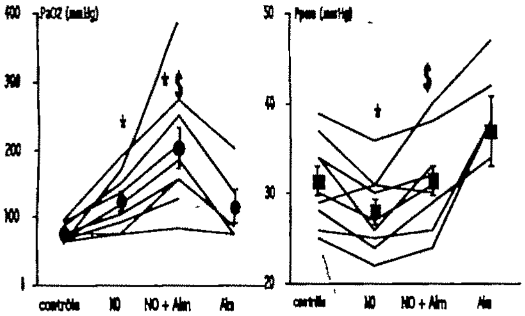
ALMITRINE MAGNIFIES THE BENEFICIAL EFFECT OF INHALED NO IN SEVERE HYPOXEMIC ARDS.

D. Payen, C. Gatecel, P. Plaisance.

Intensive Care Unit, Lariboisière University Hospital, Paris, FRANCE.

In severe ARDS, inhaled NO causes a preferential pulmonary arterial vasodilation in normal VA/Q zones, inducing a pulmonary "steal" of blood away from hypoxic vasoconstricted zones resulting in PaO_2 increase. We hypothetized that inhaled NO might be more effective if the pulmonary "steal" was increased by a potentiation of hypoxic pulmonary vasoconstriction (HPV) by almitrine. *Methods:* In 8 severe ARDS patients (Murray score=3.1±0.6; PaO_2/FiO_2=88±7 mmHg), we measured usual hemodynamic and gazometric (arterial and mixed venous) parameters: 1/ in control situation (C), 2/ after 60' NO inhalation (18ppm) (NO), 3/ 60' after association of inhaled NO and iv almitrine (6 to 16 mcg/kg/min) (NO+alm), 4/ 60' after NO withdrawal and maintened almitrine infusion (alm).

Results: Individual and mean ± sem data concerning PaO_2 and mean pulmonary arterial pressure (Ppam) are shown below. *:p<0.01 vs C, $:p<0.01 NO+alm vs NO



We observed a 2-step decrease in Qs/Qt (calculated venous admixture) from 37±1.8 to 30±1.4% (p<0.01) during NO inhalation and further to 24.7±1.3% (p<0.01 vs C, p<0.01 NO vs NO+alm) during NO almitrine association. PaO_2 increase without cardiac output impairement allowed to improve O_2 transport during NO+alm from 864±81 to 1041±79 ml O_2/min (p<0.004 vs C).

Conclusion: The dramatic increase of PaO_2 during NO inhalation and especially after almitrine infusion was in accordance with our hypothesis of a beneficial effect of HPV potentiation with almitrine during NO mediated pulmonary arterial vasodilation. These combined effects amplified the pulmonary "steal" and allowed a better matching between ventilation and perfusion. The NO almitrine association never worsened the initial pulmonary arterial hypertension. PaO_2 improvement allowed to reduce FiO_2 and PEEP levels, avoiding further O_2 toxicity and barotrauma.

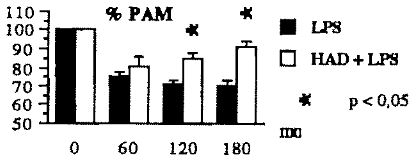
A.216

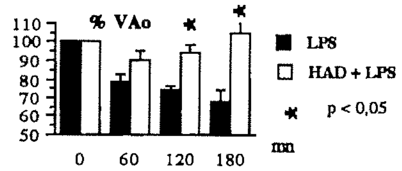
LPS ADSORPTION REVERSES IN VITRO AND IN VIVO VASCULAR DEPRESSION DURING SEPTIC SHOCK IN RABBIT.

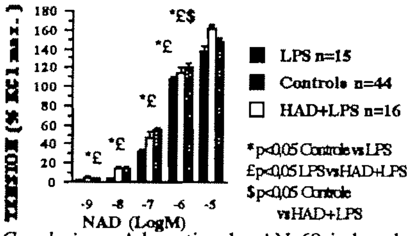
J. Mateo, B. Cholley, B. Teisseire, D. Payen;

Critical Care Unit, Lariboisiere Hospital, Paris, France.

Introduction: Lipopolysaccharide (LPS) is the starter of systemic inflammatory response in gram-negative septic shock (SS) responsible for myocardial depression and decrease in peripheral vascular tone. Many attemps concern the possibility to neutralize LPS at the early phase of SS. Among the therapeutic means, hemo-adsorption might be useful. This study has tested this hypothesis in a rabbit endotoxin shock model using HF membrane (AN 69, Hospal France).*Methods:* 20 anesthetized and ventilated rabbits were studied without any fluid resuscitation Mean arterial pressure (MAP), ascending aortic blood flow velocity (AoV) (20 MHz pulsed Doppler), blood gases and LPS plasmatic levels were measured during 180 min after LPS injection (LAL test). Animals were divided in 2 groups : 1) LPS 600 µg/Kg IVD (n=9); 2) Hemoadsorption + LPS (HAD) (n=11). HAD started before LPS injection and was maintained during 2 hours before removal.After injection a 1.5 cm segment of right carotid was removed. At the end of the experiment (3 hours after LPS) a 2 cm length intact left carotid was taken. Rings were suspended in organ chambers and a cumulative dose-response to norepinephrine (NE) (10-9 to 10-5 M) was obtained (increases in tension are expressed as percent of the maximal response to KCl.. Data were analyzed by ANOVA. *Results* : The 2 groups were not different at control. Figure shows the MAP, AoV, LPS levels and dose response curve to NE in the 2 groups







Conclusion . Adsorption by AN 69 induced a significant improvement in hemodynamic parameters. Moreover, the membrane increased LPS clearance from plasma. The in vitro study demonstrates the positive impact of a such adsorption in terms of vessel hypocontractility during sepsis.

A.217

EXHALED N-PENTANE IS NOT AN INDEX OF LIPID PEROXIDATION IN MECHANICALLY VENTILATED INTENSIVE CARE PATIENTS

H. Böhrer, A. Bach, J. Motsch, E. Martin,
D. Kohlmüller, W. Kochen

Dept. of Anaesth., Univ. of Heidelberg, and Dept. of Clin. Chem., Children's Hosp., D-69120 Heidelberg, Germany

Introduction: Lipid peroxidation which involves the formation of reactive oxygen intermediates and lipid radicals is known to occur in almost all biological systems. In recent years, the determination of exhaled n-pentane has been used to quantify the extent of *in vivo* lipid peroxidation. Intensive care patients are thought to have an increased rate of lipid peroxidation because of a multitude of factors such as oxygen therapy and intravenous lipid infusion (1,2). Aim of this study was to evaluate the significance of exhaled n-pentane in patients on long-term mechanical ventilation.

Methods: After institutional approval exhaled air was collected from 7 healthy volunteers as well as from 7 surgical intensive care patients on controlled mechanical ventilation for longer than 7 days. The air was then transferred to electropolished stainless steel bombs and analyzed as described in (3). This method is based upon cryofocusing and involves gas chromatography/mass spectrometry (GC/MS). The nonparametric Wilcoxon's rank sum test was used to compare data.

Results: Figure 1 illustrates sections of chromatograms demonstrating that n-pentane (peak 1) is not increased in intensive care patients when compared with controls. Peak 2 represents isoprene which is one of the main components of human exhaled air.

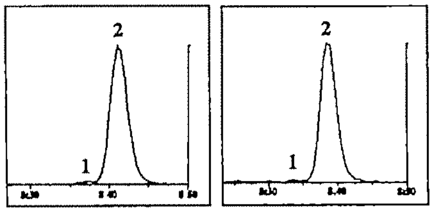


Fig. 1: Rich ion current of exhaled air samples taken from a healthy volunteer (left) and from an intensive care patient (right)

Discussion: Our findings that n-pentane is not increased in intensive care patients are in contrast to the literature. The increase in n-pentane reported by others (1, 2) may actually be due to an increase in isoprene because the commonly used analytical columns are unable to separate both substances. We have been the first to use GC/MS for identification.

Our intensive care patients were not given any vitamin E supplementation, thus avoiding suppression of increased lipid peroxidation. Assuming that oxidant stress is present in critically ill patients on mechanical ventilation, we conclude that exhaled n-pentane - when distinguished from isoprene - is not an index to assess the extent of *in vivo* lipid peroxidation in this patient population.

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1. Morita S, et al: Anesthesiology 1986; 64: 730-733.
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A.218

REACTIVE HEMOPHAGOCYTIC SYNDROME (RHS) DURING SEPSIS SYNDROME.

F. Stephan, B. Thiolière, S. Cohen, M. Tulliez, F. Clergue. Hôpital Tenon 75020 PARIS (France).

Thrombocytopenia is a frequent finding in patients with sepsis syndrome and may be associated with coagulation disorders. The purpose of this study was to identify the incidence and the prognostic value of RHS as a possible etiology of thrombocytopenia during sepsis syndrome.

Méthods: 20 patients with a sepsis syndrome (as defined by Bone criteria (1)) and a thrombocytopenia < 100×10^9/l were studied. Bone marrow aspirate was done for each patient. A percentage > 2% of activated macrophages in the marrow was required to define RHS (2).

Résults: RHS was identified in 12 patients (60%). Characteristics and studied variables are summarized in the table. Results are expressed as mean ± SEM.

variables	RHS+ (n=12)	RHS- (n=8)	p value
sex M/F	6/6	3/5	NS
age (years)	67±4.5	73±3.5	NS
APACHE II score	28±3	31±4	NS
Hb (g/dl)	10.5±0.4	10.2±0.7	NS
leucocytes (10^9/L)	12±2.5	13.5±2.9	NS
platelets (10^9/L)	65.5±8.3	64.5±9	NS
coagulopathy (n)	12	1	0.0001
Ab antiplatelets +	5	2	NS
AST (mU/ml)	660±193	203±127	0.096
bilirubin (µmol/l)	53±17	53±18	NS
creatinine(µmol/l)	219±40	143±32	NS
ARDS score (Murray)	1.75±0.4	1.57±0.3	NS
infections	75%	87.5%	NS
mortality	66%	50%	NS

Gram (-), gram (+), and fungal infections accounted for 64%, 23%, and 13%, respectively, of total infections. CMV viremia were all negative. Diagnosis for the 3 patients without clinical and bacteriological evidence of infection in the RHS group was a tumor lysis syndrome in a solid tumor, a pulmonary edema post myocardial infarction and an hæmothorax post pulmonary biopsy.

Conclusion: RHS is a common cause of thrombocytopenia during sepsis syndrome. It is always associated with coagulopathies. However, its occurence does not seem to be associated with an increased mortality.

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2): Wong K-F, Chan JKC. Reactive hemophagocytic syndrome-A clinicopathologic study of 40 patients in an oriental population. Am J Med 1992;93:177-80.

A.219

LOW HEPATIC DIHYDROPYRIMIDINE DEHYDROGENASE (DPD) ACTIVITY AND LETHAL 5-FLUOROURACIL (5-FU)-RELATED NEUROTOXICITY.

F. Stéphan*, M-C. Etienne**, C. Wallays*, G. Milano**, F. Clergue*. *Hôpital Tenon, 75020 Paris and **Centre A. Lacassagne, 06054 Nice (France).

DPD is the rate-limiting enzyme of the catabolic pathway for both pyrimidines and fluoropyrimidines (1). Cases with major toxicity -including neurotoxicity- have recently been reported in adults with deficiency in lymphocytic DPD (2,3). We report the case of a 43 years old woman with a well differenciated adenocarcinoma of the colon with multifocal hepatic metastases who developed after 5-FU chemotherapy a tumor lysis syndrome and a lethal neurotoxicity: coma with demyelination of right and left internal capsules, thalami and periventricular white matter. She had received a 2-day treatment of 2,000 mg/m2 of 5-FU by continuous i.v. infusion combined with folinic acid. 5-FU concentrations in blood and cerebrospinal fluid (CSF) and DPD activity values in liver and lymphocytes are summarized in the table.

Day after the onset of chemotherapy	5-FU concentration (ng/ml)		DPD activity (nmole/min/mg protein)	
	blood	CSF	lymphocytes *	liver **
day 10	783	566		
day 15 -before CHP	316	286	0.40	
-after 12h CHP	128	148		
day 28	ND	ND	0.35	0.09

CHP: charcoal hemoperfusion; ND: not detectable;

*: DPD activity measured in 57 head and neck cancer patients between 0.06 and 0.36, mean 0.19.

**: DPD activity measured in 8 patients without cancer between 0.10 and 0.22, mean 0.17.

This case of lethal 5-FU-related neurotoxicity suggests:
(1) a link between the low hepatic DPD activity and the very high 5-FU concentrations in blood and CSF (half-life ranges between 6 and 20 min); (2) no relation between lymphocytic DPD activity (correlated for some authors to 5-FU clearance) and hepatic DPD activity in patients with severe hepatic dysfunction; (3) the neurotoxicity was likely to be induced by the parent drug 5-FU rather than by its metabolites; and (4) CHP is effective in increasing 5-FU clearance from blood and CSF without deleterious effects.

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1): Diasio RB, Harris BE. Clinical pharmacology of 5-fluorouracil. Clin Pharmacokinetics 1989;16:215-37.
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A.220

EFFECT OF POSTURE ON RADIOLOGIC SINUSITIS IN CRITICALLY ILL PATIENTS.

P. Laurent, L. Bodin, K. Ben Jazia, M. Daghfous,
J. J. Rouby, E. Cambau, A. Zouaoui, P. Viars.
Department of Anesthesiology, Hospital of La Pitié,
University Paris VI, France.

Pansinusitis frequently complicates endotracheal intubation. The aim of this prospective and randomized study was to evaluate the effect of postural drainage on radiologic (Rx) sinusitis in mechanically ventilated patients.

Methods : From november 1991 to march 1993, after informed consent and institutional approval was obtained, 35 patients were enrolled in the study according to the following criteria : 1) orotracheal (n = 27) or nasotracheal (n = 8) intubation for mechanical ventilation, 2) presence of Rx abnormalities of maxillary (M), ethmoid (E) and sphenoid (S) sinuses defined on a paranasal CT scan as mucosal thickening, air-fluid level or complete opacification of the sinus cavity. Patients were divided into 2 groups : 16 patients were maintained in dorsal decubitus (D.D) position and 19 patients in half-sitting (H.S) position (45°) during 7 days. After randomization, endotracheal and gastric tubes were placed via the oral route in each individual. At the end of the 7-day period, a new paranasal CT scan was performed and compared to the initial CT scan by 2 independent observers. The evolution of each M, E and S sinus cavity was classified into 2 categories : Rx improvement or no Rx improvement.

Results : A total of 210 sinus cavities were evaluated (96 sinuses in D.D group and 114 sinuses in H.S group). Rx improvement (table) was observed in 18 sinuses of the D.D group (9M, 6E and 3S sinuses) and in 63 sinuses of the H.S group (23M, 26E and 14S sinuses). The difference between the 2 groups was highly significant ($p<0.001$). In the H.S group (19 patients), Rx improvement was observed in 68% of E sinuses, 61% of M sinuses ans 37% of S sinuses.

Conclusion : The study demonstrates that half-sitting position, associated with positioning tubes via the oral route, is efficient for draining M and E and, to a lesser extent, S sinuses.

Table :

	Radiologic improvement	
* p<0.001 **p<0.05	DD group (16 patients:96 sinuses)	HS group (19 patients:114 sinuses)
M sinuses	9/32	23/38**
E sinuses	6/32	26/38*
S sinuses	3/32	14/38**

A.221

PREVENTION OF NOSOCOMIAL MAXILLARY SINUSITIS IN MECHANICALLY VENTILATED PATIENTS.

L. Bodin, P. Laurent, K. Ben Jazia, M. Daghfous, J. J. Rouby, E. Cambau, A. Zouaoui, P. Viars.
Department of Anesthesiology, Hospital of La Pitié, University Paris VI, France.

Maxillary sinusitis frequently complicates endotracheal intubation. In this prospective and randomized study, the effects of the position of endotracheal and gastric tubes (nasal or oral route) on the incidence of radiologic maxillary sinusitis (Rx MS) were evaluated.

Methods : After informed consent and institutional approval was obtained, 49 patients were prospectively enrolled in the study according to the following criteria : 1) tracheal intubation for an expected duration of mechanical ventilation ≥ 7 days, 2) initial paranasal CT scan performed within 48 hours following admission to the SICU, demonstrating the absence of Rx MS (normally aerated maxillary sinuses), 3) absence of contraindications to randomization. Immediately after the initial CT scan, each patient was included in one of the 2 following groups : group I = orotracheal intubation and orogastric tube, group II = nasotracheal intubation and nasogastric tube.

After a 7-day period, a new CT scan was performed to reassess the radiologic aspects of maxillary sinuses. Rx MS was defined as the presence of an air-fluid level or a complete opacification of the sinus cavity.

Results : Among the 49 included patients, 40 patients completed the study (3 died and 6 were extubated before the 7th day). In group I (n = 18), 22% of patients had evidence of Rx MS, whereas, in group II (n = 22), 95% of patients developed a Rx MS (table).

$p < 0.001$	Presence of Rx MS (7-day CT scan)	Absence of Rx MS (7-day CT scan)
Group I (n=18) ORAL TUBES	4	14
Group II (n=22) NASAL TUBES	21	1

Conclusion : This study clearly demonstrates that the presence of intranasal tubes is a risk factor for Rx MS and that positioning endotracheal and gastric tubes via the oral route dramatically decreases the incidence of Rx MS.

A.222

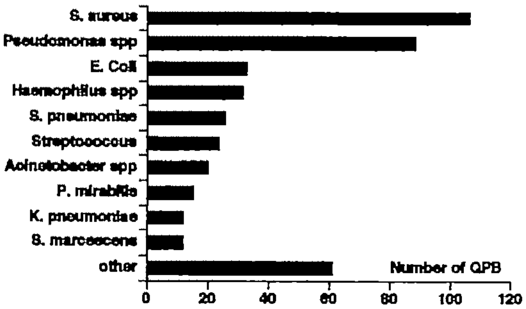
CULTURE RESULTS OF 702 PROTECTED SPECIMEN BRUSHES OBTAINED IN 688 VENTILATED PATIENTS WITH SUSPECTED NOSOCOMIAL PNEUMONIA

Claude Martin, Yves Péan, Marc Wysocki and the Study Group Bristol-Myers
Bristol-Myers Squibb, France

Background and goal of study : In order to analyse bacteria involved in nosocomial pneumonia (NP) 702 quantitative protected brushes (QPB) performed in 688 ventilated patients from 99 ICU were prospectively analyzed between Dec 92 and Feb 93.

Materials and methods : Patients were prospectively included if they had suspected NP (CDC criteria 1988) and a QPB performed according to the Wimberley technique. This study received institutional approval and informed consents were obtained.

Results and discussion : Several QPB were performed in 24 patients. Severity of the disease (SAPS, Le Gall 1984) ranged from 4 to 45 (median : 14). 143 (20 %), 287 (41 %) and 272 (39 %) of the 702 QPB were performed in patients with respectively a fatal, ultimately fatal and non fatal medical condition (McCabe 1962) and 384 (55 %) in patients with more than 1 organ failure (Knauss 1985). 364 (53 %) of the 702 QPB were obtained under antibiotherapy (ABπ), 147 (21 %) without ABπ for 7 days, 114 (17 %) while ABπ has been stopped > 2 days and 64 (9 %) ≤ 2 days. 321 (46 %) of the 702 QPB gave a culture ≥ 10^3 CFU/ml (QPB+) for at least one bacteria, 132 (19 %) were < 10^3 CUF/ml and 249 (35 %) were negative. The 321 QPB+ gave 43 bacteria (figure).



Conclusion : In this series of ICU patients, S. aureus (25 %), Enterobacteriaceae (21 %) and Pseudomonas spp (20 %) were predominant pathogens in NP diagnosed by QPB +.

A.223

PREVENTION OF CATHETER - RELATED INFECTION USING SILVER-SULFADIAZINE-CHLORHEXIDINE (SSC) BONDED CATHETERS IN AN ANIMAL MODEL

A.Bach, H.Böhrer, J.Motsch, E.Martin, H.G.Sonntag*
Dept. of Anaesthesiology and *Microbiology,
University of Heidelberg, Heidelberg, Germany

Background: Despite advances in infection control measures catheter-related infection remains a major problem in vascular access. Impregnation of catheters with silver-sulfadiazine and chlorhexidine (SSC) was tested to reduce infections *in vivo* using intravenous implantation of these catheters in rats.

Material and methods: Following insertion of either impregnated (SSC) or untreated control (C) catheters (Arrow Inc., Reading, PA) into the jugular veins of 40 rats, 10^7 colony forming units (cfu) of *Staphylococcus epidermidis* were inoculated at the cutaneous exit site. After 3 or 7 days, the catheters were removed, sonicated, and cultured quantitatively.[1] In addition, blood and samples of lung, spleen and liver tissue were cultured. Catheters were divided into 4 segments (A-D), from the intracutaneous (A) to the intravenous (D) segment.

Results: The magnitude of bacterial colonization of SSC catheter segments A to D was significantly lower (*$p<0.01$, Wilcoxon test) than of the control segments.

Bacterial colonization (mean cfu / segment ± SEM)

Group	Segment A	Segment B	Segment C	Segment D
C 3	1.5×10^6 $\pm 6.7 \times 10^5$	1.2×10^6 $\pm 8.8 \times 10^5$	5.6×10^5 $\pm 3.2 \times 10^5$	4.0×10^5 $\pm 3.5 \times 10^5$
SSC 3	$1.4 \times 10^{2*}$ ± 86	10.4* ± 10	20.2* ± 20	0.2* ± 0.1
C 7	7.6×10^5 $\pm 3.8 \times 10^5$	1.2×10^5 $\pm 5.6 \times 10^4$	2.1×10^5 $\pm 1.2 \times 10^5$	1.3×10^6 $\pm 6.0 \times 10^5$
SSC 7	$3.3 \times 10^{3*}$ $\pm 2.1 \times 10^3$	$1.3 \times 10^{3*}$ $\pm 1.1 \times 10^3$	$1.1 \times 10^{3*}$ $\pm 9.9 \times 10^2$	$1.4 \times 10^{2*}$ $\pm 1.4 \times 10^2$

The antibacterial efficacy of SSC catheters was further confirmed by a significantly lower incidence of bacteraemia ($p<0.05$) and organ colonization ($p<0.01$) in the SSC7 in comparison to the C7, and by a significantly lower incidence of organ colonization ($p<0.01$) in the SSC3 in comparison to the C3 group.

Conclusion: These data from an animal model using intravascular implantation support results obtained with simple subcutaneous implantation.[2,3] Antiseptic bonding of intravascular catheters reduces bacterial colonization and, thus, the risk of catheter-related infection.

References: 1. Antimicrobial Agents and Chemotherapy 33:1174-8,1989 2. Infection in Medicine 9:23-29,1992 3. Anesthesiology 77: A 259, 1992

A.224

ECHOCARDIOGRAPHIC ASSESSMENT OF TRAUMATIC PATIENTS

E. PHILLIPE, JP. GOARIN, M. SAADA, B. RIOU, P. VIARS
Département d'Anesthtésie-Réanimation, G.H. Pitié-Salpêtrière, 75013 Paris, France

Trauma patients need a rapid and accurate diagnosis, leading to, urgent and appropriate treatment. Recently, echocardiography has been introduced in trauma centers to give hemodynamic and anatomic information in emergency situations. The goal of our study was to prospectively evaluate the role of transthoracic (TTE) and transesophageal (TEE) echocardiography in trauma patients.

Patients and Methods

We prospectively evaluated 55 trauma patients admitted in a level 1 trauma center. The severity of trauma was assessed using the Injury Severity Score (ISS). When intubated and mechanically ventilated, patients were studied using TEE (Hewlett-Packard, Mass, USA ; Vingmed, Trondheim, Norway). TTE was performed in fully awake patients under spontaneous ventilation. All the echocardiograms were performed at the arrival in the Trauma Center by an anesthesiologist fully trained in echocardiography. Echocardiographic assessment includes hemodynamic evaluation and anatomical description of the cardiac chambers, thoracic aorta, pericardium, mediastinum and pleura. Data are mean ± SD.

Results & Discussion

Mean ISS was 29 ± 17 and mean age was 32 ± 12 yrs TEE ans TTE were performed in 36 (66 %) and 19 patients (35 %), respectively. The duration of echocardiography was < 20 min for both techniques. All images were of high quality except one TTE where no images could be obtained because of emphysema. Echocardiography was positive in 36 patients (66 %), 6 using TTE and 30 with TEE. The echocardiograms demonstrated 6 hypovolemias (4 of them resulted in shock) ; 11 myocardial contusions ; 15 hemomediastinum; 1 aortic rupture; 7 hemothorax and 3 pulmonary contusions. LV dysfunction secondary to myocardial contusion was diagnosed in 5 patients, resulting in inotropic support administration. Concerning hemodynamic instability and LV dysfunction, therapeutic decision making and follow-up were done using the echocardiographic data. No right heart catheterization was performed.

Conclusion

Echocardiography enabled rapid and accurate diagnosis at the bedside in trauma patients. Moreover, at the same time it provided hemodynamic and anatomic information, leading to adequate therapeutic intervention which were only based on echo data. Nevertheless, echocardiographic assessment in trauma patients needs well trained anesthesiologists.

A.225

INTRAVENOUS AND TRACHEAL ADRENALINE COMPARED: IMPLICATIONS FOR ADVANCED CARDIAC LIFE SUPPORT

A McCrirrick and CR Monk
Sir Humphry Davy Department of Anaesthesia,
Bristol Royal Infirmary

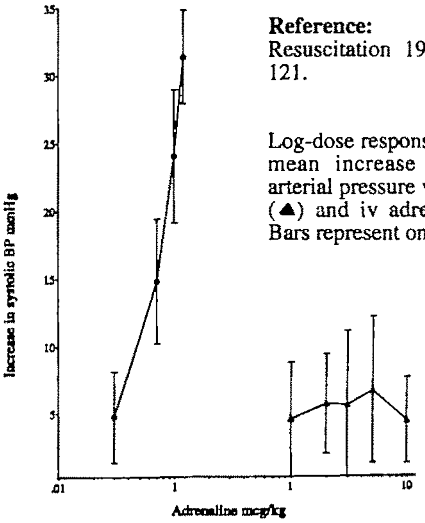
Adrenaline is the single most important therapeutic agent in Advanced Cardiac Life Support. Standard guidelines recommend 10-15 mcg/kg administered into a large central vein. The European Resuscitation Council advises that adrenaline may be given into the trachea if intravenous access is not available (1.), using twice the intravenous dose. This study established arterial pressure dose response curves for tracheal and intravenous adrenaline in humans to compare the relative efficacy of the two routes of administration.

Materials and Methods:

Informed, written consent was obtained from sixteen patients presenting for routine coronary artery bypass surgery. During elective postoperative ventilation each patient was given three doses of intravenous and two doses of tracheal adrenaline in increasing order of magnitude. The maximum doses for intravenous and tracheal administration were 0.12mcg/kg and 10mcg/kg respectively, aiming for increases in systolic pressure of under 40 mmHg. Log-dose response curves were constructed for the mean maximum increase in systolic arterial pressure.

Results and Discussion:

Tracheal adrenaline had no effect on systolic arterial pressure even at doses of 10mcg/kg. In comparison all patients who received intravenous adrenaline 0.1mcg/kg demonstrated a marked pressor response. Extensive animal research on the tracheal administration of adrenaline for resuscitation has yielded conflicting results. There is little convincing evidence from human sources to support the use of tracheal adrenaline. We believe this study provides good evidence for abandoning the tracheal route for adrenaline during Advanced Cardiac Life Support.



Log-dose response curves for mean increase in systolic arterial pressure with tracheal (▲) and iv adrenaline (●). Bars represent one SD.

Reference:
Resuscitation 1992; **24**: 103-121.

A.226

IMPROVED OUTCOME OF OUT-OF-HOSPITAL CARDIOPULMONARY RESUSCITATION

A.SCHINNERL, M ZWANOWETZ, B PONDER,.
P.LECHLEITNER °, M.BAUBIN
Universitätsklinik für Anaesthesie und Allgemeine Intensivmedizin, ° Universitatsklinik für Innere Medizin;
A-6020 Innsbruck, Anichstr.35; Austria

Prehospital cardiac arrest remains one of the great challenges for each emergency medical service (EMS) In our study the outcome of out-of-hospital cardiopulmonary resuscitation (CPR) was analyzed during two different periods of investigation. The first three years after the installation of a mobile intensive care unit (MICU) were compared with a period three years later.

Methods:

We recorded all consecutive cases of CPR by the MICU of Innsbruck in the years 1985-1988 (36 month) and 1991-1992 (14 month). Success of CPR was defined as the patients discharge from the hospital without important neurologic sequelae. Furthermore we examined the subgroup "witnessed arrest in ventricular fibrillation" analogous to the guidelines of the "Utstein style". (1)

Our MICU is staffed with an anaesthesiologist as the emergency-physician and with special trained personnel. The MICU is directed to all patients with probable vital dysfunction in the operation-area of our EMS.

Success of CPR (Survival rates):

Period 1 (1985-1988): 12 (4,4%) of 270 patients undergoing CPR had been discharged from the hospital without severe neurologic sequelae . In the subgroup "witnessed arrest in ventricular fibrillation" we found 5 survivors (9,6% of 51 patients)

Period 2 (1991-1992):19 (14,0%) of 136 patients had been discharged. In the subgroup "witnessed arrest in ventricular fibrillation" we found 13 survivors (38,2% of 34 patients).

Conclusion:

Outcome of CPR is encouraging in cases of ventricular fibrillation, but remains unsatisfying by other patients

We consider that teaching the public in basic life support (2) and teaching medical students emergency medicine systematically (3) will lead to a better CPR success in combination with permanent education of the MICU-personnel

(1) Cummins RO, Chamberlain DA, Abramson NS, et al (1991) Recommended guidelines for uniform reporting of data from out-of- hospital cardiac arrest: the Utstein style Circulation 84 960-975

(2) Cobb L, Hallstrom A, Thompson R, Mandel L, Copass M (1980) Community cardiopulmonary resuscitation. Ann Rev Med 31 : 453-462

(3) Kroesen G, Furtwängler W, Lechleitner P, Wieser Ch, Genelin A, Schinnerl A (1990) Die Integration der Notfallmedizin in das Medizinstudium. Notarzt 6 . 80-82

A.227

EVALUATION OF A PAIN THERAPY PROTOCOL IN A POST-ANESTHESIA CARE UNIT

Dan Benhamou, Selim Rahmouni, Frédéric Aubrun

Département d'Anesthésie-Réanimation - Université Paris-Sud, Hôpital Antoine Béclère, 92141 Clamart, France

Background and goal of the study : There is presently enormous interest for postoperative pain and many efficacious analgesic protocols may be used. However, it has been recently shown that intense pain frequently occurs and is insufficiently treated in the Post-Anesthesia Care Unit (PACU) (1). In the present study, pain was evaluated in a large number of PACU patients and a previously defined pain relief protocol was used and its efficacy evaluated.

Material and methods : 100 consecutive adult patients entered the study after elective orthopedic, abdominal or gynecologic surgery. Pain was evaluated using a 0-100 mm visual analog pain scale (VAPS) on arrival in the PACU and then every 15 min. When pain increased to more than 30 mm, a pain relief protocol based on the type of surgery began and was aimed at reducing VAPS to less than 30 mm. After abdominal or major gynecologic surgery, intravenous morphine was titrated up to 15 mg every 10 min by 3 mg increments and followed by propacetamol (2 grs) and then by ketoprofen (100 mg) if morphine was insufficient. After orthopedic or minor gynecologic surgery, propacetamol (2grs) was followed by morphine and then by ketoprofen (100 mg). Pain was also measured on discharge. Duration of stay in the PACU specifically dedicated to pain relief ("extra time") was defined as the difference between the time to achieve a VAPS reduction to less than 30 mm and the time theoretically necessary to achieve a safe discharge as defined by an Aldrete's score ≥ 9. Statistics included Student's t test, two way ANOVA and Chi-2 analysis as necessary and $p < 0.05$ was considered significant.

Results and discussion : Patients in this study came from orthopedic (29%), abdominal (16%) and gynecologic (55%) surgery. Anesthesia was general in 85% of cases. 25% of our patients suffered from severe pain (VAPS > 60 mm) on arrival and none on discharge. However, pain remained moderate ($20 < \text{VAPS} \leq 60$ mm) in 45% of our patients on discharge. All patients received at least one analgesic drug in the PACU and 8 % received the combination of the three drugs. The mean dose of morphine was 11.6 ± 3.0 mg and was not influenced by a previous administration of propacetamol. Extra-time dedicated to pain relief was 30.8 ± 33 min.

Conclusion : The use of this systematic pain relief protocol avoids severe pain but moderate pain still exists on discharge. The supplementary means necessary for pain therapy require cost/benefit evaluation.

References : 1 - Aubrun F. et al : Evaluation of pain and analgesia in a postanesthesia care unit. Br J Anaesth 1993; 70 (suppl 1) : A 198.

A.228

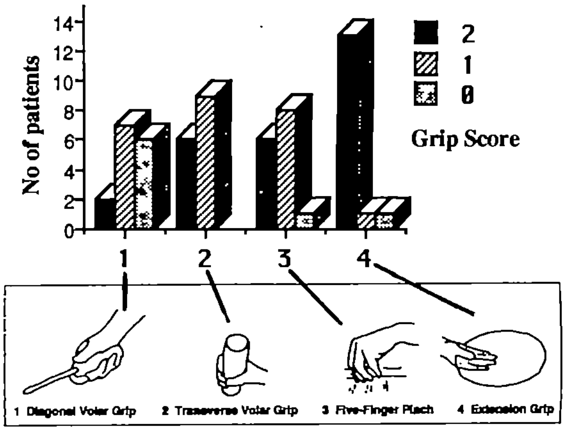
GETTING TO GRIPS WITH PCA
- AN EVALUATION OF HAND GRIP DISABILITY

Kiran JANI, Mirren TREJULLO
Dept of Anaesthesia.The Lister Hospital,
Stevenage, SG1 4AB. UK.

Background: Patient Controlled Analgesia (PCA) is a popular method of providing safe and effective postoperative pain relief. Most commercial devices require the patient to activate the pump via a demand button. We decided to evaluate two commercially available demand buttons. Graseby Adult (AB) and Graseby Paediatric (PB) in a group of patients with hand disability.

Methods: 15 patients with rheumatoid arthritic hands were tested for the performance of hand grip strength and dexterity. The patients scored 2 points if they were able to form the grip and hold onto an object being pulled away from them. 1 point was given for ability to grip but not to hold onto the object; 0 point for inability to form a grip at all. Gross motor function was assessed by recording the peak pressure generated on compressing a standardised soft bag attached to a manometer. The two demand buttons were evaluated by the patients as either easy, acceptable, difficult or very difficult to use.

Results : Patient's comments will be presented.



The lowest grip scores appear to be diagonal & transverse grip. Only 5 patients found the AB easy or acceptable to use compared with 11 patients for the PB. Only 2 patients found either the the AB or the PB easy to use.

Conclusion(s): Future designs of demand buttons must take these findings into consideration if they are not to deprive patients with hand disability from the benefits of PCA.

A.229

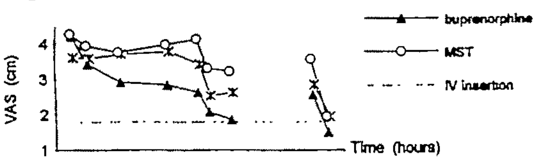
POST THYROIDECTOMY ANALGESIA: MORPHINE, BUPRENORPHINE OR BUPIVACAINE?

Louis Lacoste+, Jean Louis Kraimps*, Anne Nouzille*, Daniele Thomas+, Jacques Fusciardi+

Departments of Anaesthesiology+, Surgery* and Pharmacy*, Jean Bernard Hospital and University School of Medicine, 86021 Poitiers, France.

Background and goal of study: The goal of this double-blind study was to compare three analgesic regimens for post-thyroidectomy pain relief after general anaesthesia:pre-emptive oral controlled release morphine(MST), postoperative sublingual buprenorphine(SLB) and bupivacaine wound infiltration before skin closure.
Materials and methods: 342 patients were randomly divided into 3 groups(I,II,III) of 114 patients each. The patients received in the group I:10mg MST, 2 hours before surgery(P1), and 8 hours after the tracheal extubation(P3); in the group II:0.2mg SLB after the tracheal extubation(P2), and at P3 ; in the group III the surgeon infiltrated the wound except for laryngeal nerves with 10ml of 0.25% bupivacaine, then, medication was shifted to 0.2mg SLB at P3. The doses of MST and SLB were doubled if the age<65 years and weight>70kg. Patients were informed that they could ask for additional analgesics : opiate + propacetamol (R+P).Pain intensity was evaluated using a 0-100 mm visual analog scale(VAS) on arrival in the theatre(T-1) then 30min(T0),1h(T1),3h(T3),6h(T6),8h(T8) and 10h(T10) after P2, and on day 1 at 8h(D1T8). Each patient was asked to answer to a written satisfaction index questionary before leaving hospital. Statistical analysis included Kruskal-Wallis, Chi-Square, Fisher's exact (2 tail) tests and Anova ($p<0.05$).
Results and discussion: All groups were similar with regard to physical status, types of anaesthesia and surgery. On day 0, both R+P and VAS scores(T3,T6,T8,T10,D1T8) were lower in group II than in groups I and III. (R+P)=0.96 ± 0.84 in group I, 0.54 ± 0.68 in group II and 0.79 ± 0.78 in group III. The figure displays the consecutive VAS scores of each group. Significantly more patients in group II(96%) than in group I(85.1%) and III(91.4%) considered the analgesic regimen as satisfactory. However, 17.8% of the patients thought this surgery very painful. The side effects were not different between the groups.
Conclusion: After thyroidectomy, pain can be found and needs to be treated. The sublingual buprenorphine regimen is better than the other two regimens.

Figure: Mean VAS values



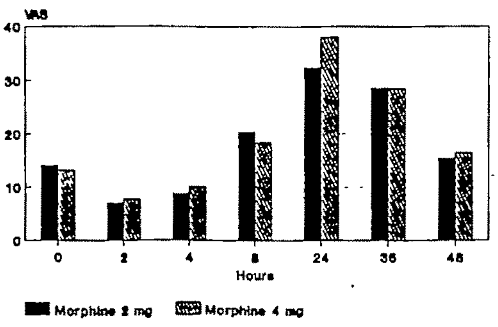
A.230

Analgesia of two doses of intraarticular morphine in day-case arthroscopy

Palle Juelsgaard, Joergen Dalsgaard, Sven Felsby
and *Johnny Froekjaer
Depts. of Anaesthesia and *Orthopaedic Surgery,
Aarhus Ámtssygehus, Aarhus University Hospital.
DK-8000 Aarhus Denmark

Introduction: The existence of peripherally distributed opioid receptors is well documented, and several studies has shown an antinociceptive effect of sub-systemic doses of morphine administered intraarticularly. An anti-inflammatory effect of morphine due to inhibition of substance P synthesis is proposed, yet a direct inhibition of nociceptive input cannot be ruled out.
Methods: 50 patients without concurrent diseases scheduled for day-case arthroscopy of the knee in infiltration analgesia were randomized to receive either 2 or 4 mg intraarticularly. The study drug was dissolved in 5 ml saline and injected via an i.m. needle after the arthroscopy. Pain intensity was assessed before surgery and 2, 4, 8, 24, 36 and 48 after injection of morphine by a VAS scale and by the consumed amount of acetaminophen. Side effects were noted if present.
Results: 47 patients completed the study. The groups did not differ in respect to demographic data, pathology or surgery. The pain scores in the two groups displayed no statistically significant difference at any time, nor did the acetaminophen consumption differ: 2609 mg/pt (2 mg), 2375 mg/pt (4 mg). No side effects were reported.
Conclusion: Earlier studies have shown significant effect of morphine after knee arthroscopy. Increasing the dose from 2 to 4 mg does not improve the analgetic effect.

VAS score
Intraarticular morphine

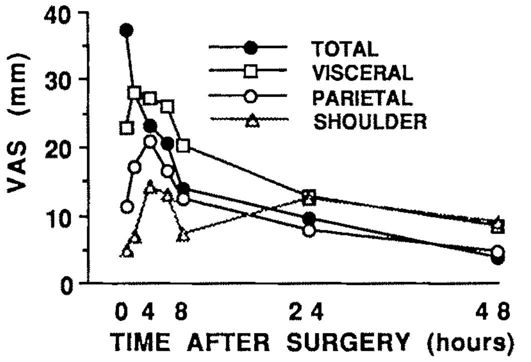


A.231

INTRAPERITONEAL BUPIVACAINE DOES NOT REDUCE POSTOPERATIVE PAIN AFTER LAPAROSCOPIC CHOLECYSTECTOMY.

E Thiry, P Paris, J Weerts[1], J Joris[2]
Department of Anaesthesiology & Intensive Care Medicine, Surgery[1] Clinique St Joseph, and Department of Anaesthesiology & Intensive Care Medicine CHU LIEGE[2], B-4000 LIEGE, BELGIUM.

Background and goal of study: Whereas patients complain more of parietal pain after laparotomy, after laparoscopy patients report visceral pain and shoulder-tip pain.[1] Intraperitoneal (ip) local anaesthetic was reported to reduce shoulder pain after laparoscopy.[2] We investigated the time course of the different components of postop pain after laparoscopic cholecystectomy and the effect of ip bupivacaine (BUPI) on these different pain components.
Materials and methods: 40 ASA I-II patients scheduled for laparoscopic cholecystectomy, and selected for their ability to differentiate the different pain components were included in this randomised double-blind study. Anaesthesia was standardised (isoflurane in 50% N_2O). At the end of surgery, 80 ml of BUPI 0.125% + Adr 1/200,000 or the same volume of saline were randomly instilled under the right diaphragm. Intensity of total pain, visceral pain (deep, dull, or resembling biliary colic), parietal pain (abdominal wall), and shoulder-tip pain were recorded on a 100 mm visual analog scale 1, 2, 4, 6, 8, 24, and 48 h after surgery. Postoperative pain was treated by dipyrone or paracetamol. Analgesic consumption was recorded during the first 48 h. Data (mean±SEM) were analysed by ANOVA , Student's *t* test, or Wilcoxon test.
Results: Demographic data (age, weight, height), duration of surgery were similar in the 2 groups (n=20). In the saline group, visceral pain was significantly more severe than parietal pain at each time point. Visceral and parietal pain were significantly greater than shoulder pain during the first 8 h postop (Fig 1).



BUPI ip did not significantly affect any of the different components of postop pain as compared with saline. Analgesic consumption was similar in the 2 groups during the first 48h postop.
Conclusions: This study confirms that visceral pain accounts for most of the pain experienced after laparoscopic cholecystectomy. BUPI ip was not effective for treating any type of pain after laparoscopic cholecystectomy.
References:1:BJA 1992;69:341, 2:Lancet 1991;338:1569

A.232

DOES THE POSITION OF THE INTRAPLEURAL CATHETER CHANGE THE RESULTS OF THE INTRAPLEURAL ANALGESIA

Janković Zorica, Palibrk Ivan

Institute of Digestive Disease, University Clinical Centre, 11000 Belgrade, Yugoslavia

Background & goal of study: Intrapleural analgesia is being used with increasing frequency for intra and postoperative pain relief in upper abdominal and thoracic surgery. The aim of our study was to determine whether the different position of the intrapleural catheter changes the onset and duration of analgesia in postoperative period.
Materials & methods: With institutional approval and patient consent we had 14 patients underwent oesophageal surgical procedures. In Group A of 7 patients intrapleural catheter was placed through the chest tube by the surgeon, tip of the catheter being placed 1 cm proximally of the top of the chest tube-at the level of the second or the third intercostal space posteriorly. In Group B of 7 patients the intrapleural catheter was placed by surgeon through the fifth intercostal space in medial line, while tip of the catheter was placed in the costodiaphragmatic sinus anteriorly (level of the tenth intercostal space). There were no differences between these two groups in body weight and height, ASA state, duration of anaesthesia and type of surgical procedure. For postoperative analgesia we used 4mg of morphine with 3mg of butorphanol diluted in 20ml of saline and applicated when the patient complained on pain. Parameters measured were: Visual Analogue Scale (VAS) score, respiratory rate, blood pressure and heart rate at 5, 10, 15, 30, 60, 90, 120, 180 and 360 minutes time intervals, onset and duration of analgesia, drowsiness and side effects.
Results & discussion: In group A the onset of analgesia started 1 to 15 min after application of analgetics (X+SD=8.43+5.59min) and in group B it was 2 to 10 minutes after application of analgesics (X+SD=5.29+3.35min). The mean time necessary to achieve minimal VAS for Group A (X+SD=62 + 54.61min) compared with Group B (X+SD=58+42.82 min). In Group A duration of analgesia varied from 145 to 1065 minutes (X+SD=518.57+369.29min) and in Group B it was from 230 to 1695 minutes (X+SD=746.43 + 535.48 min). The differences between these two groups were not statistically significant (Student's t-test). In both groups arterial pressure and heart rate did not change significantly. Side effects which followed this combination of analgesia were swelling, nausae and halucinations during the dream, but they were rare.
Conclusion: Although Group A had later onset of analgesia, longer time to achieve minimal VAS score, shorter duration of analgesia and shorter time to onset and longer lasting drowsiness, none of these differences were statistically significant. The distance between the tips of the intrapleural catheters in our two groups was 6 to 8 intercostal spaces and one was positioned anteriorly and the other posteriorly, it had no influence on onset, duration of analgesia, vital parameters and side effects. This result agrees with the evidence that the position of the patient during the injection of the intrapleural analgesics has no influence on analgesics distribution. Our study shows that distribution of the intrapleurally injected analgesics is independent of the position of the tip of the intrapleural catheter.

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2. Baker J. and Tribble C., Pleural Anaesthetics Given through an Epidural Catheter Secured Inside Chest Tube. Ann Thorac Surg Vol 51: 138-139,1991

A.233

EPIDUROSCOPY WITH A THIN FLEXIBLE AND DEFLECTABLE FIBRESCOPE

P.H. Rosenberg, J.E. Heavner, S. Chokhavatia, K. McDaniel, G.B. Racz

Department of Anaesthesiology, University of Helsinki, Finland, and Departments of Anesthesiology and Physiology Texas Tech University, Lubbock, Texas, U.S.A.

Background and goal of the study: A realistic anatomical image of the epidural space may be obtained by direct endoscopy ex vivo (1) or in vivo. The recent development in fibreoptic and video imaging technology is a major step towards future diagnostic and therapeutic use of thin flexible epiduroscopes.

Material and methods: After institutional review board approval epiduroscopy was performed in anaesthetized dogs. A 40-cm or 80-cm flexible fibrescope (Karl Storz, OD 2.3 mm, 3Fr working channel, 180° deflectable tip) was inserted via laminectomy at lumbosacral or upper lumbar level. Fibreoptic and fluoroscopic images were captured on a MAC IIci computer and recorded on video tape. Instruments for dilatation, electric stimulation, tissue sampling and suction were passed through the working channel and tested.

Results: In canine epidural space the instruments could be passed under visual control up to the cervical level without motor or cardiovascular (EEG, heart rate) responses. The view, which was better at withdrawal of the scope, could be improved by air or saline injection. Blood vessels were readily identified and haemorrhage was minimal. Small foreign bodies, introduced via separate interspaces, were located and identified. Epidural fat, in particular at lumbar level, limited visualization.

Conclusion: Direct viewing of the epidural space (also subarachnoid space) is significantly improved by available modern technology. Before human clinical use, refinement of orientational guides on the instrument is needed.

Reference: 1. Blomberg R. A method for epiduroscopy and spinaloscopy. Acta Anaesthesiologica Scandinavica 1985;29: 113-116.

A.234

COMPARISON OF ONDANSETRON, DROPERIDOL AND SALINE FOR PREVENTION OF NAUSEA AND VOMITING WITH PATIENT CONTROLLED ANALGESIA FOLLOWING ORTHOPAEDIC SURGERY.

R ALEXANDER, D SEINGRY

DEPARTMENT OF ANAESTHESIA, ROYAL NATIONAL ORTHOPAEDIC HOSPITAL, STANMORE, MIDDLESEX, UK

Background and goal of study: The use of patient controlled analgesia (PCA) (1) and orthopaedic surgery (2) are both associated with a high incidence of postoperative nausea and vomiting (PONV).This double-blind randomised study compares the efficacy of ondansetron (group O), a 5HT-3 antagonist, to that of droperidol (group D) and saline (group S) in the prevention of PONV following major orthopaedic surgery when using PCA morphine postoperatively.

Materials and Methods: 77 ASA 1 and 2 patients were given a standardised general anaesthetic (premedication; temazepam 0.3mg/kg, induction; thiopentone 2.5-5mg/kg and vecuronium 0.1mg/kg, and maintenance; nitrous oxide 66% in oxygen with Enflurane 1-2%). Analgesia was provided with morphine. At the end of surgery group O received ondansetron 4mg stat and 8mg added to 50mg morphine, group D received droperidol 1.25mg stat and 5mg added to 50mg morphine and group S, nil added to 50mg morphine. The trial mixtures were diluted to 50mls with 0.9% N/Saline. PCA bolus dose was set at 1ml, four hour maximum dose at 30mls and the lockout time at 5 min. Nausea and vomiting scores, sedation scores, frequency of rescue anti emetic (metoclopramide 10mg) administration and the amount of morphine consumed, were recorded hourly over 24hrs by nursing staff.

Results: There was no population difference in weight, age, gender, length of anaesthetic for each group or the amount of morphine administered over 24hrs.

	n	no symptoms (%)	nausea (%)	vomiting (%)
S	27	4 (15) [5]	6 (22)	17 (63)
D	26	11 (42) [11]	5 (20)	10 (38)
O	26	19 (73) [20]	4 (15)	3 (12)

[Number of patients not requiring rescue treatment]

The incidence of vomiting and request for rescue treatment were significantly lower with ondansetron compared to droperidol ($P<0.05$).

Conclusion: Ondansetron is a superior anti-emetic than droperidol in preventing PONV associated with PCA morphine following major orthopaedic surgery.

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A.235

PREMPTIVE ANALGESIA WITH KETOROLAC IN ORTHOPAEDIC SURGERY : A DOUBLE BLINDED RANDOMIZED STUDY.

D Fletcher, P Zetlaoui, S Monin, K Samii

Anesthesiology Dept, Université Paris Sud, Hôpital de Bicêtre,
94275 Bicêtre, FRANCE.

Background: Premptive analgesia is a recent concept. This study evaluated the preemptive analgesic effect of intravenous (IV) ketorolac (K) for total hip replacement (THR).

Materials & methods : After approval of the local Ethic Committee, 50 patients operated under general anesthesia for a THR were randomally allocated to three groups. In all groups, two double blinded intravenous injections were done before induction and at the end of the surgery. The control group (CONT; n = 15) received 2 ml of normal saline (NS) for both injections. The preoperative K group (PRE ; n = 18) received 60 mg of ketorolac then 2 ml of NS. The postoperative K group (POST ; n = 17) received 2 ml of NS then 60 mg of K. General anesthesia was standardized. The pain was controlled in the recovery room (RR, Ho) with an intravenous titration of morphine (Mo) (2 mg / 5min until the pain is tolerable). The patients used a PCA pump (ABBOTT) in the surgical ward (bolus : 1 mg, lockout time : 10 min). The visual analog scale scores at rest and movement were evaluated hourly for 6 hours then every 6 h for two days. The side effects monitered were : sedation, respiratory depression, nausea, perioperative bleeding. The statistical analysis used ANOVA, Student's t test, Mann Whitney U test, Chi square test. A value of $p < 0.05$ was considered significant. Data are expressed as mean ± SEM.

Results (table) : The characteristics of patients and surgery were similar in the three groups. The EVA score at rest for the PRE group is diminished compared to the CONT and POST group at H0. The EVA score at rest is diminished in the POST group compared to the CONT group at H0. Beyond H0, the EVA scores at rest and movement are similar in the three groups. Cumulative doses of morphine (CDM) in CONT and POST groups are similar. CDM in the PRE group are decreased compared to the CONT group from H0 to H18 and compared to the POST group from H0 to H12. Two patient in the PRE group one in the POST group had abnormal bleeding. Two patients in CONT group and two in POST group had severe sedation and respiratory depression after titration.

Conclusion : In this study 60 mg of preoperative K had an analgesic effect superior to the same dose administered at the end of the surgery. This effect is important in the immediate postoperative period but is not sustained with time.

Table :

Groupe	Pre	Post	Cont
EVA H o	41 ± 7 ** / *	60 ± 6 §	74 ± 7
EVA H 1	30 ± 20	36 ± 24	46 ± 20
Titration (mg)	3 ± 1 ** / *	10 ± 1	12 ± 1
Morphine H 12 (mg)	11 ± 2 ** / *	23 ± 2	26 ± 3
Morphine H 48 (mg)	51 ± 6	63 ± 9	52 ± 4

**: $p < 0,05$ Pre vs Post *: $p < 0,05$ Pre vs Cont
§: $p < 0,05$ Post vs Cont ; m ± SEM, test U de Mann Whitney.

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Title: KETOROLAC TROMETHAMINE FOR POSTOPERATIVE ANALGESIA IN ORAL SURGERY.

Authors: Ph. E. Pendeville, M. J. Van Boven, V. Contreras and H. Reychler.
Affiliation: UCL Medical School, Saint-Luc Hospital, Brussels, Belgium.

Introduction: Ketorolac tromethamine, a parenteral non-steroidal anti-inflammatory drug is currently being assessed as a postopérative analgesic. This study was designed to examine the efficacy and safety of single dose i.v. ketorolac 30 mg compared with placebo after third molar removal.

Patients & methods: After approval of the protocol by the Ethical Committee of the UCL Medical School, sixty patients ASA I-II were randomly allocated to receive placebo or ketorolac tromethamine 30 mg during the induction of anesthesia for oral surgery. Anesthesia was induced with i.v. propofol, alfentanil and maintained with propofol; atracurium was used to obtain neuromuscular block.

Each patient also received i.v. methylprednisolone 125 mg and ampicilline 1 g during surgery. An observer, who was blinded to which group the patient was included, evaluated pain (VAS), edema and mouth opening at 1, 2, 6 and 24 hrs after surgery.

Results are expressed on mean ± SD. Student' *t* test was used for comparison of the patient groups and *ANOVA* repeated measures was used for analysis of VAS, edema and mouth opening.

Results & discussion: The groups are comparable with regard to age, sex, height, weight, ASA status, duration of anesthesia and surgery, time to awakening and dose of alfentanil. The patients in the ketorolac group experienced significantly less pain than in the placebo group up to 24 hrs ($p < 0.001$) (*fig.1*). Edema was also less important in the ketorolac group ($p < 0.001$) (*fig.2*) but the difference was not statistically significant concerning mouth opening.

No side effect was recorded in this study. Oral surgery is often performed on a daycare basis despite the problems of pain and edema. Ketorolac could be an useful alternative to morphine for providing analgesia without risk of respiratory depression. Our results confirm the results of an other recent study and suggest an interesting synergy between NSAIDs and SAIDs (ref.2) .

In conclusion, this study demonstrates that an intraoperative dose of ketorolac 30 mg i.v. improves postoperative comfort during the first 24 hrs after surgery by lowering pain and edema.

fig.1

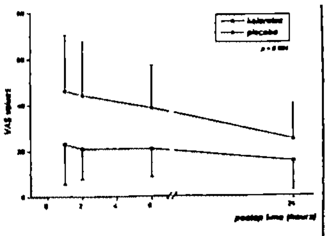
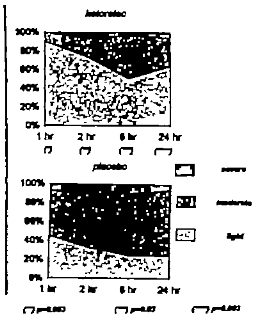


fig.2



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A.237

TITLE:A COMPARISON OF THE EFFECT OF INTRA MUSCULAR DICLOFENAC,KETOROLAC,OR PIROXICAM ON POSTOPERATIVE PAIN FOLLOWING LAPAROSCOPY.

Authors: O'Hanlon J., Milligan K., Beers H.,Huss B.
Affiliation:Lagan Valley Hospital, Lisburn,Co. Antrim, BT28 1JP,N. Ireland.

Background&goal of the study: During laparoscopic instrumentation of the uterus and fallopian tubes prostaglandins are released,therefore non-steroidal anti-inflammatory drugs(nsaids), by inhibiting prostaglandin production, should decrease postoperative discomfort; reducing opiate requirement[1].Both diclofenac and ketorolac demonstrate a morphine sparing effect after surgery[2,3]. The aim of this study was to determine the analgesic properties of piroxicam as compared to diclofenac and ketorolac.

Methods: With ethical approval and informed consent, 60 ASA 1-11 patients were studied. All patients were free from systemic illness and concurrent non-steroidal medication. Preoperatively a visual analogue scale(VAS) of 0-10 cm was explained to the patient. Following a standard anaesthetic technique of;propofol 2mg/kg,fentanyl 1mcg/kg,atracurium 0.3mg/kg and maintenance with 1-1.5% isoflurane in 60% nitrous oxide;patients were randomly allocated to diclofenac(D),ketorolac(K)or piroxicam(P) groups. Receiving an intramuscular injection of diclofenac 75mg, ketorolac 30mg or piroxicam 20mg respectively. Postoperatively pain was assessed by VAS: on admission to recovery ward,1hour post-op,2 hours post-op,4 hours post-op and at 24 hours post-op. The time to first analgesia was also noted.

Results:Patient characteristics and operation details were similar in the three groups. There was no significant differences between the three groups p<0.005. There was difference in time to first analgesia:group D 27(93.7)mins, group K 16.3(30.2)mins and group P 61.9(120)mins. In group D 14 patients didn't require further analgesia,group K 11 patients and group P 10 patients.

VAS scores

	0	1hr	2hrs	4hrs	24hrs
group D	0	3.2(3.2)	2.6(2.7)	2.1(2.4)	0.6(1.5)
group K	0	2.4(3)	2.8(3.1)	2.4(3.2)	0.95(1.9)
group P	0	2.8(2.5)	2.6(2.3)	3(2.9)	0 65(1.2)

Conclusions: Piroxicam 20 mg when given as an intramuscular injection compares favourably with ketorolac and diclofenac in respect to: VAS scores,number of patients not requiring further analgesia and time to first analgesia .

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A.238

TITLE: COMPARATIVE EFFECT OF KETOROLAC AND KETOPROFEN ON A NOCICEPTIVE FLEXION REFLEX IN HUMANS

AUTHORS: X. Dupont, MD, C.Menigaux, MD, C.Lebrault, MD, P.Alfonsi, MD, P. Malassine, MD, M. Esteve, MD, M.Chauvin, MD.
AFFILIATION: Anes. Dept., Ambroise Pare Hospital, 92104, Boulogne, France

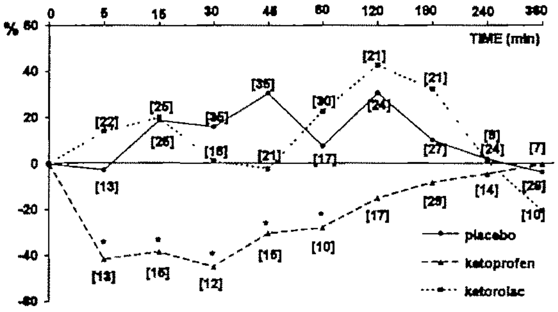
Background and goal of study : Besides their well known peripheral action, a central component of the analgesic effect of NSAIDs has also been demonstrated (1). However, NSAIDs seem to have differential mode of action (2). Intrathecal administration of ketorolac suppressed the phase 2 response of the formaline test in the rat (3). But, the hypothesis of the central analgesic effect of intravenous ketorolac in humans has not been tested. Therefore, the aim of this study was to investigate the effect of ketorolac, administered intravenously, and to compare it to ketoprofen and a placebo, on the lower limb nociceptive flexion reflex (RIII), in volonteers in a double-blind study.

Materials and methods : 7 consenting healthy male volunteers received placebo (10 ml saline), ketorolac 60 mg or ketoprofen 200 mg in 10 ml saline during 3 different experiments. RIII reflex was studied according to a method previously described (3). Recruitment curves were obtained to calculate the slope of the curve and the threshold (Tr) of the reflex before (control) and 5,15,30,45,60,120,180,240 and 360 min after IV injection. Data were expressed in terms of percentage of control values and reported as mean ± SEM. Statistical analysis used paired or unpaired Student's t-test as required.

Results and discussion: There were no significant changes in Tr after ketoprofen, ketorolac or placebo. The slope of the recruitment decreased significantly ($p < 0.05$) during 1 hour (fig) after ketoprofen compared to placebo whereas ketorolac had no significant effect on this parameter.

Our data support previous results showing a central action of ketoprofen (4). However, the observed effect is a reduction in the amplification of RIII reflex without change in Tr. By contrast, the lack of inhibition of RIII reflex with this large dose of ketorolac strongly suggests that ketorolac is without any effect on the spinal reactivity following IV injection.

Fig 1: Time course of slope changes expressed as a percentage of difference from baseline. P< 0.05 ketoprofen versus placebo.



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A.239

EFFECTS OF METOCLOPRAMIDE ON A NOCICEPTIVE FLEXION REFLEX IN HUMANS

Menigaux C, MD, Dupont X, MD, Alfonsi P, MD, Estève M, MD, Lebrault C, MD, Chauvin M, MD

Anes. Dept., Ambroise Pare Hospital 92104 Boulogne France

Background & Goal of the study: Recent studies (1,2) have suggested an analgesic action of metoclopramide showing a decrease in the use of common analgesic drugs. In order to define more precisely this analgesic property we realized a double blind randomised study to compare the effects of metoclopramide or placebo on the nociceptive flexion reflex in healthy volunteers.

Materials & methods: Following approval by the local ethical committee, 6 consenting healthy male volunteers (28-41 yr., 60-80 kg) were enrolled in the study. R III reflex was studied according to a method previously described (3). the sural nerve was stimulated at its retro-malleolar pathway and electromyographic (EMG) reflex responses were recorded from the ipsilateral biceps femoris muscle using surface electrodes. The study protocol was the following: after iv access two recruitments (increasing intensity was applied in order to obtain a recruitment curve of the R III as the function of the stimulus intensity, allowing the calculation of the slope and the threshold) were realized at five min interval and served as a control value (represented by the mean of the two values of slope and threshold). Then a stimulation at constant intensity of 1,2 threshold was applied during 40 min. **After 10 min** each subject received **either placebo** (10 ml saline) or **metoclopramide** (10 mg in 10 ml saline water intravenously). At the end 2 recruitments were realised. The pain was quantified using EVA at each recruitment and just before the injection and 30 min after. Data are expressed in term of percentage of the control value and reported as mean ± sem. We used a paired or unpaired Student's t test as required for the slope and threshold and a non parametric Wilcoxon test for the EVA.

Results & Discussion: Recruitment results are summarised in the table. R III curve under constant intensity remained stable. EVA pain score did not differ with control value.The R III is transmitted by Aδ fibers. So metoclopramide at this dose did not have any synaptic effect in the spinal reflex. The lack of analgesia excluded also the possibility of supra -spinal action.

Δ %	placebo	metoclopramide
threshold	+6,7% ± 18,2	+2,8% ± 10,1
slope	+1,6% ± 14,2	- 3,4 % ± 28,1
EVA	- 2,5% ± 9,3	+ 2,5% ± 10,5
	NS	NS

Δ %: variation in % with control value

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A.240

ANALGESIC EFFECTS OF EPIDURAL KETAMINE AND CLONIDINE FOR POSTOPERATIVE PAIN RELIEF

A Chiari, G Redl, W Menth, R Berger, W Klimscha

Department of Anesthesiology, University of Vienna
Währinger Gürtel 18-20, A-1090 Vienna, Austria

Introduction: Epidural clonidine is known to produce postoperative analgesia (1). Epidural ketamine has analgesic properties too, although small doses seem to be inadequate (2). An advantage of both drugs is that motor function is not impaired. The purpose of this study was to assess the efficacy, safety and appropriate dose of epidural clonidine and ketamine for postoperative analgesia.

Patients and Methods: After institutional approval 35 patients who underwent orthopedic lower limb surgery were randomly allocated in 5 groups. Following insertion of a lumbar epidural catheter patients recieved general anesthesia for surgery. For postoperative analgesia they recieved epidurally either 0,2 mg/kg ketamine (k1-group), 0,4 mg/kg ketamine (k2-group), 0,2 mg/kg ketamine + 2 μg/kg clonidine (k1+c-group), 0,4 mg/kg ketamine + 2 μg/kg clonidine (k2+c-group) or 2 μg/kg clonidine (c-group).

Analgesia was assessed using the VAS pain score every 5 minutes for 30 minutes, thereafter every 15 minutes for 6 hours. Duration of analgesia was defined as the time elapsed between epidural injection of ketamine/clonidine and first complaint of pain. In this case we administered 5 ml of bupivacaine 0,25% to provide further analgesia. Maximum pain relief was determined by Δ% reduction in VAS pain score.

Vital signs (heart rate, blood pressure, respiratory rate and arterial oxygen saturation) were recorded continuously. For statistical evaluation ANOVA and student's t-test were used. A p-value < 0,05 was considered significant.

Results: Analgesic effects of ketamine were dose dependent in terms of intensity of pain relief and duration. Combination of clonidine with ketamine significantly improved duration or intensity of pain relief (Table 1). Mild hypotonia occured with administration of clonidine but none of our patients required vasopressor treatment. No case of respiratory depression was observed.

Discussion: Ketamine or clonidine administered epidurally have limited analgesic properties whereas the combination of these two drugs seems to be a safe and effective technique to obtain a profound and long acting postoperative analgesia leaving motor function intact.

Table 1 mean ± sem

GROUP	k1	k2	k1+c	k2+c	c
Baseline VAS	7,4 ± 0,8	8,4 ± 0,3	7,3 ± 0,9	8 ± 0,7	7,3 ± 0,9
Max pain relief Δ%	53 ± 8,7	75 ± 12	87 ± 9*	74 ± 7	64 ± 8
Duration of action (min)	95 ± 20	100 ± 13	180 ± 26*	212 ± 32*	222 ± 58*

* significantly different from k1 and k2 group

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A.241

NITROUS OXIDE AS AN ANALGESIC FOR PAINFUL PROCEDURES OUTSIDE THE OPERATING THEATRE

Anki Notini Gudmarsson

Department of Anaesthesia and Intensive Care, Danderyd Hospital, Danderyd, Sweden

Background and goal of study: The analgesic property of nitrous oxide is widely recognized for alleviation of pain during child birth, in dental service and in ambulance care (1). Many patients, however, sustain painful albeit short-lasting diagnostic and therapeutic interventions without adequate pain relief. We decided to investigate whether nitrous oxide could be an effective, practical and safe alternative for analgesic therapy in these situations.

Material and methods: 60 women undergoing minor gynecological procedures under local anaesthesia in the outpatient department were randomized to breathe either air or prefabricated mixture of 50 % nitrous oxide in oxygen (Medimix®, AGA Gas AB, Stockholm, Sweden) through mask. Time to mobilization was measured. In a subsequent study 68 patients scheduled for notoriously painful procedures (e.g. bone marrow biopsy), or refusing continuation of painful intervention (e.g coloscopy) had Medimix® administered for pain relief. In these patients arterial oxygen saturation was followed by pulse oximetry. Pain was evaluated by visual analogue scale. All patients (128) were assessed by the investigator concerning performance and possible side effects. A patient questionnaire was answered concerning general wellbeing.

Results and discussion: No untoward reactions occurred. All patients had a smooth and almost instantaneous recovery without nausea or womiting. In the first study the Medimix® patients got to their feet and left the room earlier than the controls No arterial desaturation was descovered. Medimix® reduced pain in all patients. 54 patients assessed their pain as more than 50 (scale 1 to 100). 37 patients had a 50 % decrease in pain score.

Conclusions: Quality care requires effective procedures to combat acute pain in all forms. Medimix® has proven easy to use, effective and safe. We believe it has a definite niche in the analgesic arsenal. With appropriate education and training the treatment can be administered by non anaesthesia personell.

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A.242

Symptomatic Pain Management for Patients with Sclerodermia

L. Radbruch, D. Zech, S. Grond, T. Meuser, K.A. Lehmann

Department of Anaesthesiology, University of Cologne, Köln, Germany

Background: In the treatment of non-tumour associated pain syndromes, opioids are often not used because of the high incidence of opioid-nonresponsive pain and the fear of tolerance with prolonged administration. We present three cases of sclerodermia-induced pain treated successfully with oral opioids for 1 - 17 months.

Material & methods: In the years 1992-93 three patients with progressive sclerodermia were treated in our pain clinic. Two patients had visceral manifestations, one patient cutaneous symptoms only.

Results & discussion: Patient 1 (female, 52 years) suffered severe soft tissue pain on the trunk caused by contractions of the skin. Under treatment with slow release morphine in increasing doses (60-180 mg/day), first in combination with non-opioid analgesic drugs (dipyrone and naproxen) and later as a monotherapy, numeric analog scores (NAS) were reduced from 60 to 20. Because of the rapid progression of the disease therapy with monoclonal antibodies against t-cells was induced in the dermatological department, and with the slow regression of disease symptoms it was possible to reduce morphine doses. 15 months after antibody therapy no further morphine was required and the patient remained pain free.

Patient 2 (male, 44 years) had ischemic pain in the left foot from an necrotic ulcer on the second toe. An intravenous guanethidin-block resulted in pain relief lasting 8 hours, but a neurolytic sympathetic block was refused by the patient. Oral tramadol and naproxen reduced pain intensity from NAS 100 to 50. After amputation of the necrotic toe the patient was pain free, even after morphine was discontinued 46 days after admission.

Patient 3 (female, 63 years) was admitted in the pain clinic 9 years after the first diagnosis of sclerodermia. She reported pain from multiple body sites, caused by contractions and ulcerations of the skin. Causal therapy with penicillamine had been stopped because of renal dysfunction. Analgesic therapy with oral naproxen and tramadol reduced pain intensity from NAS 90 to 50, with mild to moderate gastrointestinal side effects. The patient was lost to follow-up 42 days after admission.

Conclusions: As with cancer pain management, symptomatic therapy with oral opioids provides good pain relief for patients with sclerodermia even in long-term treatment. Reduction of analgesic requirements and sometimes complete pain relief may be obtained by treatment of the underlying cause of pain.

A.243

NIMODIPINE DOES NOT POTENTIATE ORAL MORPHINE IN CANCER PAIN. A PRELIMINARY STUDY

G. Roca, J.L. Aguilar, V. Mazo, F. Vidal
Anaesthesia Department. Pain Clinic.
Badalona University Hospital
Universidad Autónoma de Barcelona. SPAIN

BACKGROUND AND GOAL OF THE STUDY:
Experimental data suggest a true pharmacological potentiation between calcium channel-blockers and morphine. The aim of this study was to assess the therapeutic efficacy as co-analgesic, of 30 mg/8h oral nimodipine added to individual oral slow release morphine (MST) in patients with cancer pain.

MATERIAL AND METHODS:
This is a prospective, randomised, double-blind, cross-over, placebo-controlled study. Twenty four patients with oncologic pain receiving MST and having pain scores > 4 on a 10 cm visual analog scale were included.
Timing: The study lasted 8 days. Patients randomly received MST + placebo (P) or nimodipine (N)(30 mg/8h) during three days. During two days they only received MST, and finally, in a cross-over fashion MST + nimodipine or placebo. The most important exclusion criterium was NO intake of another drug except MST.
Variables studied: age, sex, height, weight, kind of neoplasm, type of pain (nociceptive/neuropathic), location, and intensity, pain relief and mood measured all on a 10 cm visual analog scale (VAS), and Verbal categoric scale (validated in Spanish),three times a day. Quality of sleep was recorded once a day. Goldberg's test and Beck's depression index were answered by all patients. MST doses were not varied throughout the study.

RESULTS:

	PAIN	RELIEF	MOOD	VERBAL	SLEEP
BASAL	6.4	2.8	5.7	2.7	4.5
	(1.6)	(2.8)	(2.8)	(0.9)	(3.0)
P	3.6**	5.7**	6.4^{ns}	5.3**	6.3*
	(2.2)	(2.8)	(2.0)	(2.4)	(2.1)
N	3.5**	5.9**	6.1^{ns}	5.6**	5.6^{ns}
	(1.8)	(2.3)	(2.3)	(2.3)	(2.2)

mean (SD);ns:not significant;*:$p<0.05$;** $p<0.01$

CONCLUSION:
1.- Oral nimodipine 30 mg/8 h does not potentiate the analgesic action of slow release morphine in patients with cancer pain.
2.- Both nimodipine and placebo added to MST significantly decreased pain scores when compared with basal values, emphasizing the importance of placebo effect in patients with cancer.

A.244

LONG-TERM CONTINUOUS INTRATHECAL ADMINISTRATION OF MORPHINE/BUPIVACAINE AT THE UPPER CERVICAL LEVEL FOR PAIN DUE TO PROGRESSIVE INTRA-ORAL CANCER. ACCESS BY A LATERAL CI-II APPROACH.

B.J.P. Crul*, R.T.M. van Dongen*, D.G. Snijdelaar*, E.H.J.M. Rutten**.

* Pain Clinic, Department of Anesthesiology and ** Department of Radiotherapy, University Hospital, Nijmegen,
The Netherlands.

Continuous intrathecal (IT) administration of a morphine/bupivacaine mixture is advocated for the management of incident and neurogenic types of cancer pain (1). For optimal efficacy the tip of the catheter should be as near to the pain conducting nerves as possible (2). In patients suffering from orofacial cancer, pain is often conducted by the upper cervical and the ninth and tenth cranial nerves and sometimes difficult to treat with oral analgesics. Catheter insertion at the CI-II level is described allowing positioning of the catheter tip in the vicinity of the pain conducting nerves.

Methods
The technique is slightly modified from the lateral intrathecal approach used in percutaneous cervical cordotomy. In the supine patient under fluoroscopic guidance a 20 G Tuohy needle is inserted in a slightly caudo-cranial direction aiming at the anterior part of the cervical intrathecal space at the CI-CII level. The projection of the entrance place of the needle through the skin should correspond with the arch of second cervical vertebra, the tip of the needle piercing the dura just behind the caudal part of the arch of the first cervical vertebra. After obtaining a free flow of CSF the catheter is advanced with the bevel turned cranially about 5 cm intrathecally and tunneled subcutaneously along the course of the sternocleidomastoid muscle to the infraclavicular region.
Two patients were treated.

Results and discussion
Patient A, female, 50 yr, incurable progressive T4M0N0 intraoral squamous cell carcinoma. Notwithstanding maximal treatment with oral analgesics she suffered from attacks of severe stabbing pain in the right ear, VAS 9-10. Installment of an IT catheter at the CI-II level. IT infusion of morphine, starting dosage morphine 0.5 mg/24h gradually increased over a five day period to 7.2 mg/24h. Only after adding bupivacaine 15 mg/24h a VAS 5 was obtained. No side effects.
Patient B, female, 52 yr T4M1N1 intraoral squamous cell carcinoma. Pain attacks left ear, pain during swallowing, VAS 7-8. IT infusion at CI-II level. Partial pain relief (VAS 5) during morphine 2.9 mg/24h. Dizziness and vertigo after adding bupivacaine 10 mg/24h. Full pain relief (VAS 0-1) and no side effects during bupivacaine 6.6 mg/24h.
In both patients injection of contrast dye proved the catheter tip was positioned close to the foramen magnum.
These results support the following assumptions:
1. CI-II intrathecal infusion is a feasible technique in cancer patients with severe neurogenic pain in the upper neck region.
2. IT morphine/bupivacaine is effective for the treatment of incident pain.

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Papers for publication and all editorial communications should be addressed to:
Professor G. Smith,
Editor, British Journal of Anaesthesia,
University Department of Anaesthesia,
Leicester Royal Infirmary,
Leicester LE1 5WW.
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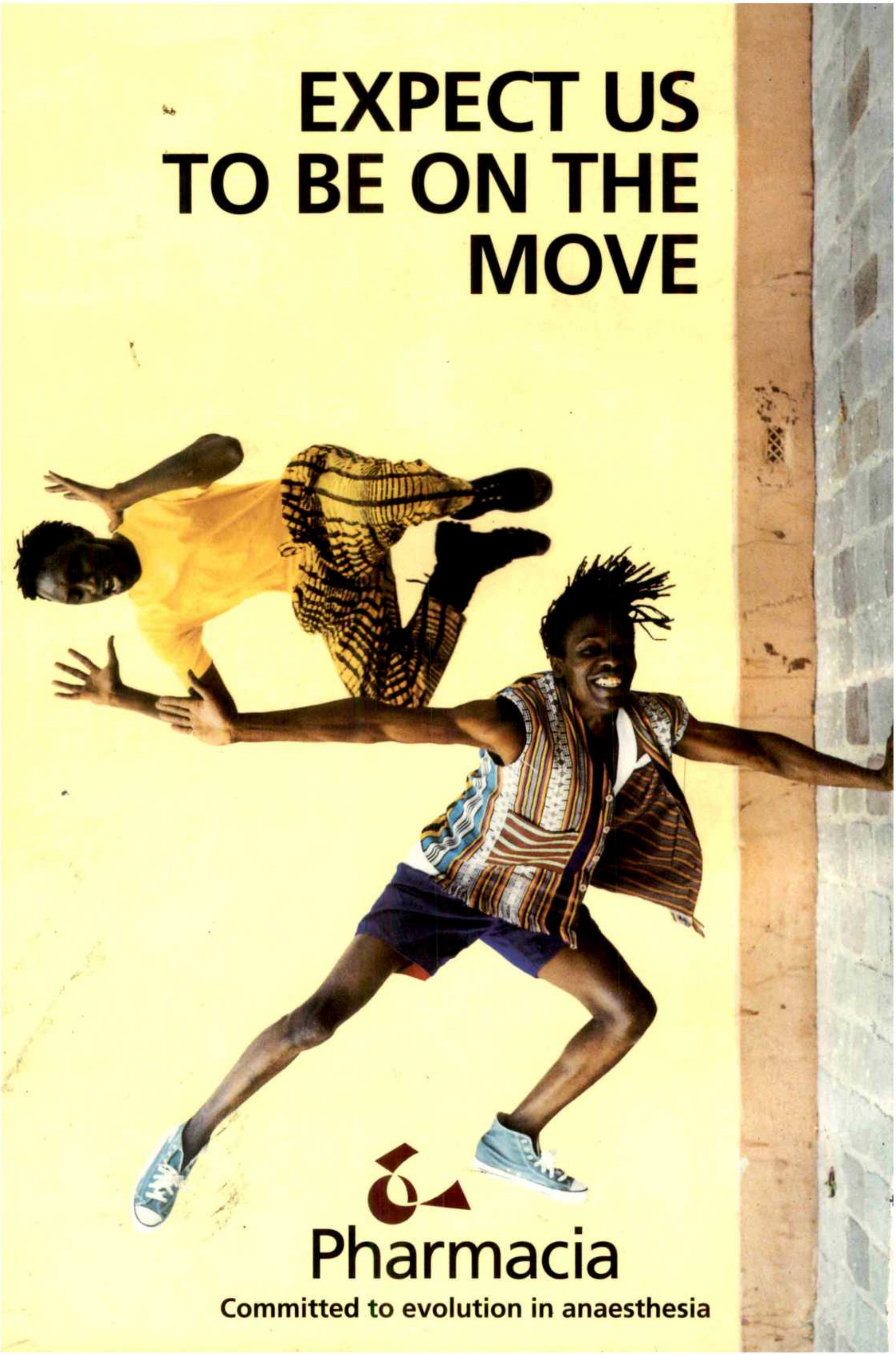
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Papers for publication and all editorial communications should be addressed to:
Professor G. Smith,
Editor, British Journal of Anaesthesia,
University Department of Anaesthesia,
Leicester Royal Infirmary,
Leicester LE1 5WW.
Telephone: 0533 470141
Fax: 0533 854487

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